EPA Registration File
53883-312

Material Sent for Data Extraction

Reg. # 53883-312

Description: _____

☐ Material(s) Sent to Data Extraction Contractors:

- ☑ New Stamped Label Dated 9/5/13
- ☐ Notification Dated _____
- ☐ New CSF(s) Dated _____
- ☐ Other: _____

☐ Decision #: _____

☐ Other Action/Comments: _____

_____

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Autumn Metzger

Phone: 305-5314 Division: RD - IRB

Date: 9/5/13

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

SEP 0 5 2013

Control Solutions
c/o James Messina, Exponent
1150 Connecticut Avenue, N.W.
Suite 1100
Washington, DC 20036

Dear Mr. Messina:

Subject: Amendment to revise restriction under "Directions for Use" to read "Do not use on dogs or puppies under [6.5/6½][23][45][89] pounds or less than 8 weeks of age."
CSI Fipronil + Novaluron Spot-on for Dogs
EPA Registration No. 53883-312
Your Submissions Dated 8/30/2013

The labeling referred to above submitted in connection with the Federal Insecticide, Fungicide and Rodenticide Act, as amended is acceptable.

A stamped copy of the labeling is enclosed for your records. Please submit one final printed copy of the labeling before releasing the product for shipment. If you have any questions regarding this label, please contact Autumn Metzger at (703) 305-5314 or metzger.autumn@epa.gov.

Sincerely,

Reuben Baris
Acting Product Manager (07)
Insecticide-Rodenticide Branch
Registration Division (7505P)

{FRONT LABEL}

CSI Fipronil + Novaluron Spot-On for Dogs

[For use only on dogs 8 weeks of age or older]
[For use only on dogs 8 weeks old and older]
[For use only on dogs more than 8 weeks old]
[For use only on dogs [&][and] puppies 8 weeks or older and 6.5/6½ lbs. and over]
[For use only on dogs 6.5/6½ lbs. and over [and][&] over 8 weeks of age]
[Only apply to puppies over 8 weeks old]
[Only apply to puppies 8 weeks or older]
[Apply to dogs 8 weeks of age or older]
[Apply only to dogs 8 weeks of age or older]
[Apply to dogs >8 weeks old]
[Apply only on dogs [and puppies] [>6.5/6½ lbs./more than 6.5/6½ lbs. [and/&] over 8 weeks old]

{One of following will be used on label}
[For use ONLY on dogs [&][and] puppies]
[ONLY for Dogs & Puppies 8 weeks or older [and][&] 6.5/6½[-] [to] 22 lbs]
[6.5/6½[-] [to] 22 lbs] [Only for Dogs 6.5/6½[-] [to] 22 lbs.]
[23[-] [to] 44 lbs] [Only for Dogs 23[-] [to] 44 lbs.]
[45[-] [to] 88 lbs] [Only for Dogs 45[-] [to] 88 lbs.]
[89[-] [to] 132 lbs] [Only for Dogs 89[-] [to] 132 lbs.]
[over 8 weeks of age]]
{or}
[Only for Dogs 6.5/6½-22 lbs. & Puppies (8 weeks or older)]
[Only for Dogs 23-44 lbs.]
[Only for Dogs 45-88 lbs.]
[Only for Dogs 89-132 lbs.]

ACCEPTED
SEP 0 5 2013
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under:
EPA. Reg. No: 53883-312

ACTIVE INGREDIENTS:

Fipronil	9.8%
Novaluron	20.0%
OTHER INGREDIENTS:	70.2%
TOTAL:	100.0%

{1.5 cm x 1.5 cm or as listed below/bottom right corner of front panel}

KEEP OUT OF REACH OF CHILDREN
CAUTION

[See [Back][or][Side] [Label[s]] [Panel[s]] [or] [insert] for Additional Precautionary Statements]

{Option 1: Net Contents related to specific CRP packaging}
NET CONTENTS: X fl oz [Y – X fl oz applicators]
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][Twenty-Four] 0.023 fl oz (0.67 mL) applicators
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][TwentyFour] 0.045 fl oz (1.34 mL) applicators
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][Twenty-Four] 0.091 fl oz (2.68 mL) applicators
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][Twenty-Four] 0.136 fl oz (4.02 mL) applicators
{End Option 1}

{Option 2: Net Contents related to specific CRP packaging}
NET CONTENTS: X fl oz [3 – X fl oz applicators]
[[Three] [3] 0.023 fl. oz. (0.67 mL) applicators]
[[Three] [3] 0.045 fl. oz. (1.34 mL) applicators]
[[Three] [3] 0.091 fl. oz. (2.68 mL) applicators]
[[Three] [3] 0.136 fl. oz. (4.02 mL) applicators]
{End Option 2}

{Front label may include various marketing statements, refer to Optional Marketing Language section}

{END FRONT LABEL}

{BACK LABEL}

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 8 WEEKS OF AGE.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS. CAUTION: Harmful if swallowed. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

FIRST AID	
If swallowed	• Immediately call a poison control center or doctor. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Have person sip a glass of water if able to do so. • Do not give anything by mouth to an unconscious person.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. [You may also contact [XXX-XXX-XXXX] for emergency medical treatment information.]

HAZARDS TO DOMESTIC ANIMALS. For external use on dogs only. Individual sensitivities, while rare, may occur after using any pesticide product on dogs. If signs of sensitivity occur bathe your dog with a mild soap and rinse with large amounts of water. If signs persist, or become more severe within a few days of application, consult a veterinarian immediately. If your dog has an unusual reaction to the initial application, consult a veterinarian before repeating treatment. Certain medications can interact with pesticides. Consult a veterinarian before using on medicated, known organ dysfunction, debilitated or aged dogs. [Call [XXX-XXX-XXXX] for 24-hour assistance.]

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT ALLOW CHILDREN TO APPLY PRODUCT. TO PREVENT HARM TO YOU AND YOUR DOG, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. Do not have contact or allow children contact with treated area until completely dry.

Do not use on dogs or puppies under [6.5/6½][23][45][89] pounds or less than 8 weeks of age. Do not allow your dog to ingest this product. Use entire contents of tube on each dog. Do not split one tube between dogs. Do not use multiple tubes on one dog. Weigh your dog to be sure you are applying the right dose formulated for the weight of your dog. Do not treat your dog with more than one pesticide product at a time. Do not use on rabbits or animals other than dogs. Do not use on pregnant or lactating dogs. Separate the treated dog from all other dogs and cats for 24 hours after treatment has been applied.

Side Effects: Monitor your dog after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Individual sensitivities, while rare, may occur after using any pesticide product. If signs persist, or become more severe within a few days of application, consult a veterinarian immediately. If your dog has an unusual reaction to the initial application, consult a veterinarian before repeating treatment. Certain medications can interact with pesticides. [Call [XXX-XXX-XXXX] for 24-hour assistance.]

DO NOT USE ON CATS. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.

{1.5 cm x 1.5 cm or as listed below/bottom right corner of back panel}

[Optional drawings that may or may not appear anywhere on finished label]

[[Application Instructions] [How to Apply - May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.[

Only For Dogs Weighing 6.5/6½[-][to[22 lbs. [including small dogs and puppies,] 8 weeks or older
[For cartons containing 0.023 fl. oz. (0.67 ml) applicator tubes]
Apply one [tube] [applicator] (0.023 fl. oz.) (0.67 ml) [as a spot [on][to] the dog's back between the shoulder blades][from the back of the neck to a point midway between the neck and tail].

Only for Dogs Weighing Between 23[-][to]44 lbs.
[For cartons containing 0.045 fl. oz. (1.34 ml) applicator tubes[
Apply one [tube] [applicator] (0.045 fl. oz.) (1.34 ml) [as a spot [on][to] the dog's back between the shoulder blades] [from the back of the neck to a point midway between the neck and tail].

Only for Dogs Weighing Between 45[-][to]88 lbs.
[For cartons containing 0.091 fl. oz. (2.68 ml) applicator tubes]
Apply one [tube] [applicator] (0.091 fl. oz.) (2.68 ml) [as a spot[on][to] the dog's back between the shoulder blades] [from the back of the neck to a point midway between the neck and tail].

Only for Dogs Weighing 89[-][to]132 lbs.
[For cartons containing 0.136 fl. oz (4.02 ml.) applicator tubes]
Apply one [tube] [applicator] (0.136 fl. oz.) (4.02 ml) [as a spot [on][to] the dog's back between the shoulder blades] [from the back of the neck to a point midway between the neck and tail].
Do not use two tubes on dogs greater than 132 lbs.

FREQUENCY OF APPLICATION
Use [Brand Name] monthly for control of flea, tick, flea egg, [and] chewing lice [and mosquito] infestations. [Studies show that] [Brand Name] kills adult fleas for up to three months. Apply monthly if your dog is at high risk for flea reinfestation[, or in a highly infested environment]. [Apply monthly to kill mosquitoes within 24 hours.] Apply monthly to control ticks[,] [mosquitoes] and chewing lice. Do not reapply for [30 days][4 weeks].

[If you have questions or comments about this product, please write: CSI Consumer Response, 5903 Genoa-Red Bluff Road, Pasadena, TX 77507]

[In Case of Emergency, call: XXX-XXX-XXXX]
[For more information]
[Non-Emergency, call XXX-XXX-XXXX]
[Made in USA]

[Distributed by:][Manufactured by:]
Control Solutions, Inc.
5903 Genoa-Red Bluff Road
Pasadena, TX 77507

EPA Reg. No. 53883-312
EPA Est. No. XXXXX-XX-XXX

{END BACK LABEL}

{FOLLOWING TEXT MAYBE FOUND ON SIDE PANELS, BACK PANEL AS SPACE PROVIDES OR PRODUCT INSERT}

{Option 1: How to open label language related to specific CRP packaging}
[Option 1a]
How to open: Remove product tube[s] [vial] from the package. [Separate one tube from the others.] Hold the tube [vial] with notched end pointing up and away from the face and body of you and your dog. Use scissors to cut off the narrow end at the notches along the line.

How to apply: Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. [Do not apply more often than once every 4 weeks.] [Repeat application may be made if necessary, but do not apply more often than once every 30 days.] [Repeat application [may][can] be made every four weeks.]

[Option 1b]
How to open

1. Remove product tube[s] [vial] from the package.
2. [Separate one tube from the others.] Hold the tube [vial] with notched end pointing up and away from the face and body of you and your dog. Use scissors to cut off the narrow end at the notches along the line.

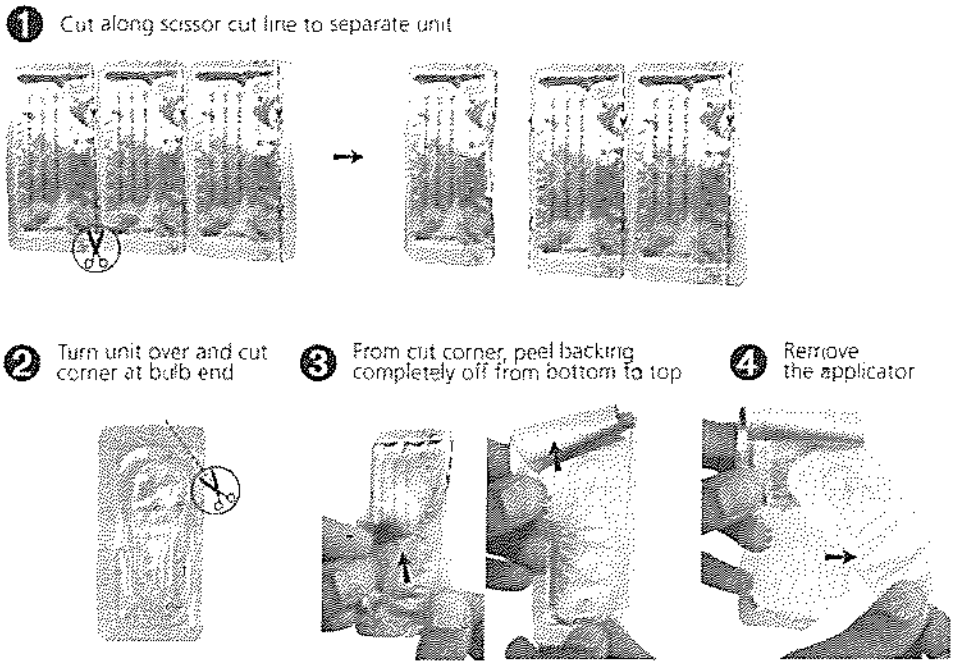
How to apply

1. Invert tube over dog and use open end to part dog's hair.
2. Squeeze tube firmly to apply all of the solution to the dog's skin [as a spot [on][to] the dog's back between the shoulder blades.] [or] [from the back of the neck to a point midway between the neck and tail.]

{End Option 1}

{Option 2: How to open label language related to specific CRP packaging}

DIRECTIONS FOR OPENING PACKAGING:



{End Option 2}

[Brand Name] contains fipronil and the insect growth regulator (IGR) novaluron. [Brand Name] effectively targets fleas and ticks. [Brand Name] features a sustained release formula created to act fast and provide [long lasting] control of fleas, ticks, flea eggs, [mosquitoes] and chewing lice for up to [1 month] [[four] [4] weeks] [30 days]] on dogs.

STORAGE AND DISPOSAL

PESTICIDE STORAGE: Do not remove tube from the pack until ready to use. Store in a cool [below 77°F[/] (25°C)] dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: If empty: Non-refillable container. Do not reuse or refill this container. Offer for recycling if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

[LIMITATION OF WARRANTY AND LIABILITY

Read the entire direction for use, conditions of warranties and limitations of liability before using this product. If terms are not acceptable, return the unopened product container at once. By using

this product, user or buyer accepts the following **CONDITIONS, DISCLAIMER OF WARRANTIES**, and **LIMITATIONS OF LIABILITY**.

CONDITIONS: The directions for use of this product are believed to be adequate and must be followed carefully. However, it is impossible to eliminate all risk associated with the use of this product. Animal injury, ineffectiveness or other unintended consequences may result because of such factors as presence of other materials, or the manner of use or application, all of which are beyond the control of Control Solutions, Inc. To the extent consistent with applicable law, all such risks shall be assumed by the user or buyer.

DISCLAIMER OF WARRANTIES: To the extent consistent with applicable law, Control Solutions, Inc. makes no other warranties, express or implied, of merchantability or of fitness for a particular purpose or otherwise, that extend beyond the statements made on this label. No agent of Control Solutions, Inc. is authorized to make any warranties beyond those contained herein or to modify the warranties contained herein. To the extent consistent with applicable law, Control Solutions, Inc. disclaims any liability whatsoever for special, incidental or consequential damages resulting from the use or handling of this product.

LIMITATIONS OF LIABILITY: To the extent consistent with applicable law, the exclusive remedy of the user or buyer for any and all losses, injuries or damages resulting from the use or handling of this product, whether in contract, warranty, tort, negligence, strict liability or otherwise, shall not exceed the purchase price paid or at Control Solutions, Inc. election, the replacement of product.]

[If you have questions or comments about this product, please write: CSI Consumer Response, 5903 Genoa-Red Bluff Road, Pasadena, TX 77507]

[In Case of Emergency, call: XXX-XXX-XXXX]
[For more information]
[Non-Emergency, call XXX-XXX-XXXX]
[Made in USA]

[Distributed by:][Manufactured by:]
Control Solutions, Inc.
5903 Genoa-Red Bluff Road
Pasadena, TX 77507

EPA Reg. No. 53883-312
EPA Est. No. XXXXX-XX-XXX

[Look at the Label [Look at the Label icon] 6 Step [Spot-On] [Squeeze-On] [Topical] Checklist

- Read the label completely and follow directions
- Weigh your dog
- Do NOT use Dog products on Cats

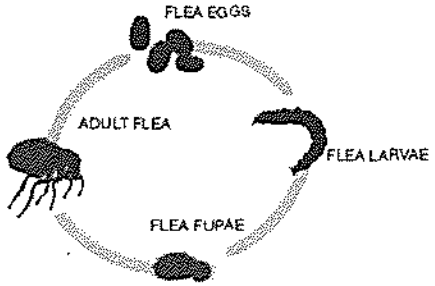
- Do NOT treat with more than one pesticide product at a time
- Separate animals after treatment for at least 24 hours to avoid chance of ingestion
- Do NOT split tubes between Dogs [and use the ENTIRE tube contents].]

[**Brand Name**]
[1][2][3][4][5][6][12][24] [Month [Treatment] [Application] Tracker]
[Monthly reminder card]
[Apply [Brand Name] monthly for continuous protection against fleas, ticks, flea eggs [and] chewing lice [and mosquitoes].]
[For year-round protection, apply [**Brand Name**] monthly.]
[Pet's Name (Empty blank for owner to fill in name)]
[First][1st][Second][2nd][Third][3rd][Fourth][4th][Fifth][5th][Sixth][6th][Seventh][7th][Eighth][8th][Ninth][9th][Tenth][10th][Eleventh][11th][Twelfth][12th]
[Dose] [Treatment] [Application]
[(Empty blank for owner to fill in date)(Date: MM/DD/YY)]
[Calendar stickers with brand name] [Place stickers on your calendar as a reminder to reapply [brand name] in 30 days.]

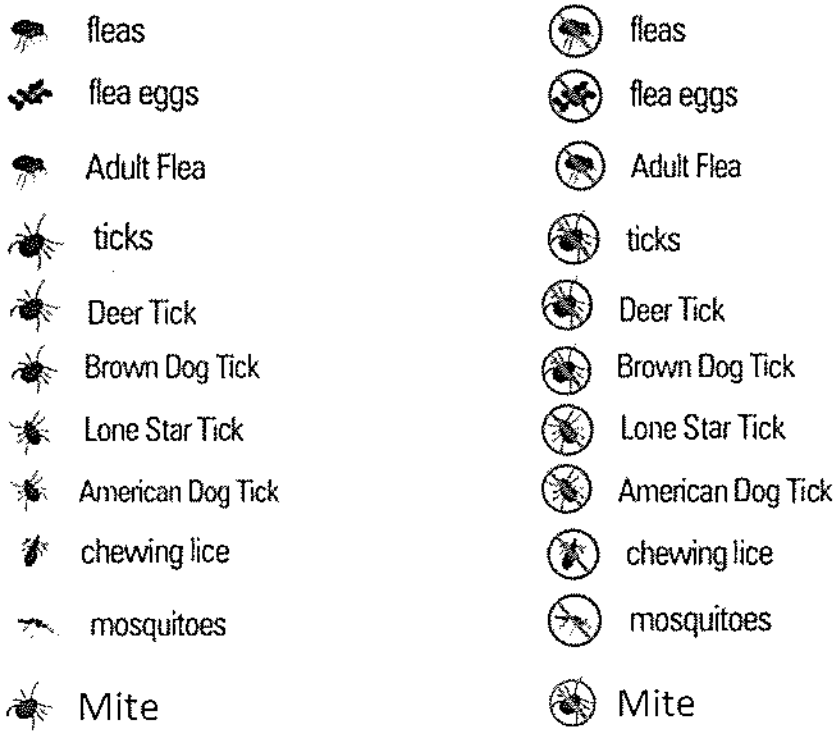
[Monthly Application Reminder Magnet]
[Enclosed for your convenience is an application reminder magnet. Push the (reset) button to start the clock. After 30 days the magnet will flash (and beep) reminding you to reapply [Brand Name]. This application reminder can be used for future treatments. Just press the reset button and in another 30 days the reminder magnet will flash (and beep) reminding you to reapply.]

{END: TEXT THAT MAYBE FOUND ON SIDE PANELS, BACK PANEL AS SPACE PROVIDES OR PRODUCT INSERT}

{Optional graphics below may or may not appear anywhere on finished label}



[Flea life cycle diagram] [Flea Life Cycle]
[Sample coloring and layout may be different on final label]



{End optional graphics}

{TUBE / VIAL LABEL}

{Option 1 Tube label related to CRP Option 1}

Front Label	Back Label
Brand Name {cat graphic with line through it} **Use only on dogs 8 weeks and older and [6.5/6½-22][23-44][45-88[[89-132] lbs.** Fipronil 9.8%, Novaluron 20.0% w/w [0.023 fl oz **(or)** 0.045 fl oz **(or)** 0.091 fl oz **(or)** 0.136 fl oz] [label code]	KEEP OUT OF REACH OF CHILDREN CAUTION: Read directions and precautions before using. Use scissors to open. EPA REG. No. 53883-312 [label code]

{End Option 1}

{Option 2 Blister pack label related to CRP Option 2}

{START – BLISTER PACK INFORMATION}

{END – BLISTER PACK INFORMATION}

Front Label	Back Label
Brand Name {cat graphic with line through it} **Use only on dogs 8 weeks and older and [6.5/6½-22][23-44][45-88][89-132] lbs.** Fipronil 9.8%, Novaluron 20.0% w/w [0.023 fl oz **(or)** 0.045 fl oz **(or)** 0.091 fl oz (or) 0.136 fl oz] [label code]	KEEP OUT OF REACH OF CHILDREN CAUTION: Read directions and precautions before using. EPA REG. No. 53883-312 [label code]

{End Option 2}

[OPTIONAL MARKETING LANGUAGE THAT MAY BE FOUND ON ANY PANEL OR INSERT OF THE LABEL OR PACKAGING]

[**Fleas**]
[• Research demonstrates that [brand name] kills adult fleas and flea eggs for up to one month]
[• [Brand Name] prevents development of fleas for up to one month]
[• Prevents adult fleas and flea eggs]
[• If dog is a high risk for flea reinfestation, a once a month application is needed]
[• Kills flea eggs for up to 1 month]
[• With Novaluron Insect Growth Regulator which Breaks the Flea Life Cycle]
[• With Novaluron to Break Flea Life Cycle]
[• With Insect Growth Regulator to Break Flea Life Cycle]
[• Dual Action [!]:Fipronil with Novaluron IGR Effectively Breaks the Flea Life Cycle]
[• Dual Action [!]: Effectively Breaks the Flea Life Cycle[!]]
[• Kills Fleas Up to [4 weeks][1 month][30 days]!]
[• Prevents Flea Eggs From Developing Into Biting Adults]
[• Breaks the flea life cycle]
[• Effectively kills adult fleas and flea eggs]
[• Kills adult fleas [for up to three months]]
[• Kills newly emerged adult fleas before they lay eggs]
[• Kills adult fleas, which may cause [flea allergy dermatitis] [and][or] [flea bite anemia]]
[• Kills Fleas]
[• Kills Flea Eggs]

[**Ticks**]
[• Kills Ticks]
[• Kills ticks including those that may transmit Lyme disease]
[• Kills Ticks for Up to [4 weeks][1 month][30 days]!]*
[• Kills [all stages of] deer ticks [(which may be a vector of Lyme disease)][(including those that may transmit Lyme disease)] for up to [4 weeks][1 month][30 days]]
[• Kills all stages of deer ticks]
[• Kills Ticks (including deer ticks) for up to [4 weeks][1 month][30 days]]
[• Kills [brown [dog ticks],] [American [dog ticks],] [and] lone star [ticks]] [dog ticks] [and] [deer ticks] [(*Rhipicephalus sanguineus*)] [for up to [4 weeks] [1 month][30 days]]]
[• Kills American dog ticks [(*Dermacentor variabilis*)] for up to [4 weeks][1 month][30 days!]
[• Kills ticks that may transmit Lyme disease, Rocky Mountain spotted fever, ehrlichiosis, babesiosis, and anaplasmosis]

[**Mosquitoes**]
[• Kills mosquitoes] [within 24 hours for up to 7 days] [and] [within 48 hours for up to 28 days]

[Multiple Pests]
[• Flea & Tick Control for Dogs & Puppies 8 weeks old and older]
[• Kills fleas, flea eggs, ticks, chewing lice [& mosquitoes][for up to 4 weeks][30 days]1 month]]
[• Controls flea reinfestation for up to [4 weeks][four weeks][one month]]
[• Kills fleas, ticks, [mosquitoes,] chewing lice and flea eggs][for up to] [1 month][30 days][4 weeks]]
[• Monthly flea, tick, [mosquito], chewing lice, and flea egg protection]
[• Monthly flea, tick, [mosquito] and chewing lice protection]
[• Kills fleas, ticks, [mosquitoes], flea eggs and chewing lice]
[• [Six] [6] [5][Five] Way Protection [Kills fleas, ticks, [mosquitoes], [mites], chewing lice and flea eggs]]
[• [5] [Five] [Four][4] Way Protection! Kills fleas, ticks, [mosquitoes], chewing lice, [and] [&] flea eggs]
[• [4 Week] [1 month][30 day][Flea and Tick [Treatment][Application]]
[• [Four (4) Week] [Flea, Tick, [Mosquito,] [flea egg,] and chewing lice control]
[• 4 week Flea and Tick Treatment!]
[• Once A Month Flea and Tick [Treatment][Application]]
[• Kills Fleas and Ticks for up to 4 weeks!]
[• When used monthly [brand name] completely breaks the flea life cycle and controls tick and chewing lice infestations.]
[• Use [Brand Name] monthly to control fleas, ticks, [mosquitoes], flea eggs [and chewing lice]]
[• Kills Fleas, Ticks & Flea Eggs for up to 4 Weeks]

[Other]
[• Only for Dogs and Puppies 8 weeks of age or older]
[• Can only be used on puppies 8 weeks of age and older]
[• Formulated for Dogs and Puppies 8 weeks of age or older]
[• Only for Dogs [6.5/6½-22 lbs], [23-44 lbs], [45-88 lbs], [89-132 lbs]
[• Fast Acting]
[• Long Lasting]
[• Once a month treatment]
[• Convenient and simple spot treatment]
[• Convenient spot treatment]
[• A once monthly application is required for chewing lice]
[• Rapidly eliminates infestations of chewing lice]
[• Rapid elimination of chewing lice infestation[s]]
[• Kills chewing lice][and aids in the control of mites that may cause sarcoptic mange]
[• Aids in Control of Sarcoptic Mange]
[• Controls mites that cause sarcoptic mange]
[• [X] Applications {for cartons with [X] applicators}] and/or [[X] Month Supply] or [[X] Week Supply]
[• Best if used year round!]

[• For year-round protection, apply [Brand Name] monthly]
[• (ICON Showing 4 Week Protection)]
[• 4 Week Dose!]
[• 1 Month Dose!]
[• 30 Day Dose!]
[• Easy to Use [Application]]
[• Formulated for Dogs and Puppies over 8 weeks of age]
[• Patented Technology]
[• Apply once every [4 weeks][month][30 days]!]
[• Repeat application [may][can] be made every four weeks.]
[• Apply monthly]
[• Fipronil (9.8%) + Novaluron (20.0%)]
[• Prevents and controls reinfestation[s] of listed pests [for 4 weeks] [for 1 month][for 30 days]]
[• Stops existing infestations of listed pests]
[• Prevents [establishment of additional infestation] [infestation of listed pests] [for] [1 month][4 weeks][30 days]]
[• Lift here for more information]
[• [One Application][Two Applications][Three Applications][Four Applications][Five Applications][Six Applications][Twelve Applications][Twenty-Four Applications] and/or [1 Month Supply][2 Month Supply][3 Month Supply][4 Month Supply][5Month Supply][6 Month Supply][12 Month Supply][24 Month Supply] or [4 Week Supply][8 Week Supply][12 Week Supply][16 Week Supply][Twenty Week Supply][24 Week Supply][48 Week Supply][52 Week Supply][104 Week Supply]]
[• [1][2][3][4][5][6][12][24] Applications]
[• Contains Fipronil[,] [-]the [same] active ingredient used in Frontline® brand products*]
[• Contains Fipronil[,] [-]the [same] active ingredient used in the leading competitive brand[s]]
[• *[Brand Name] is not manufactured by or distributed by Merial. Frontline® is a registered trademark of Merial.]
[• [Brand Name] is a trademark of [**Company Name**]]

Metzger, Autumn

From: James Messina [jmessina@exponent.com]
Sent: Friday, August 30, 2013 3:46 PM
To: Metzger, Autumn
Cc: Anne Turnbough (aturnbough@ControlSolutionsInc.com)
Subject: EPA Label Amendment
Attachments: 53883-312 Fipronil Novaluron Label 8-30-2013 clean.pdf; 53883-312 Label Amendment 8-30-2013.pdf

Autumn,

Thank you for taking the time to talk with me today regarding the CSI label. As discussed, please find attached the label amendment to add correct the one statement weights. We have only made this change and added the EPA Registration Number to the label. We look forward to working with you and will wait to hear back from you on processing. We appreciate all of your efforts.

Have a great weekend.

Best Regards,

James Messina
Principal Regulatory Consultant
Exponent
Center for Chemical Regulation and Food Safety
1150 Connecticut Avenue, N.W.
Suite 1100
Washington, DC 20036
202-772-4932
202-772-4979 fax
301-908-1181 cell

CSI
CONTROL
SOLUTIONS
incorporated
A Makhteshim-Agan Company

August 30, 2013

John Hebert
Product Manager 7
Office of Pesticide Programs (7504P) (AMEND)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: **Fast Track Label Amendment for CSI Fipronil + Novaluron Spot-On for Dogs (EPA Registration Number 53883-312)**

Dear Mr. Hebert:

Control Solutions, Inc. (CSI, 5903 Genoa Red Bluff, Pasadena, TX 77507-1041, EPA Company Number 53883), is submitting a fast track label amendment to the EPA approved product CSI Fipronil + Novaluron Spot-On for Dogs (EPA Registration Number 53883-312), containing the EPA registered active ingredients fipronil (9.8%) and novaluron (20%). The following information is included in support of this amendment:

- Transmittal Document;
- Application for Amendment (EPA Form 8570-1); and
- Revised label (3 copies: 1 track changes, 2 clean).

CSI is submitting an amendment to revise label language to reduce the potential for misuse of the product by a consumer. We have only added the EPA Registration Number and the following sentence has been updated on page 3: "Do not use on puppies under [6.5/6½][23][45][89] pounds and 8 weeks of age." No other changes have been made to the label.

If you have any questions or need additional information, please contact me at atumbough@controlsolutionsinc.com or at 281-892-2532.

Sincerely,

Anne M. Turnbough

Anne Turnbough Ph.D.
Director, Regulatory Affairs

RECEIVED

Enclosures

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States Environmental Protection Agency Washington, DC 20460

☐ Registration ☒ Amendment ☐ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number 53883-312	2. EPA Product Manager John Hebert	3. Proposed Classification ☒ None ☐ Restricted
4. Company/Product (Name) Control Solutions, Inc./CSI Fipronil + Novaluron Spot-on for Dogs	5.PM# 7	

5. Name and Address of Applicant *(Include ZIP Code)*
Control Solutions, Inc.
5903 Genoa Red Bluff
Pasadena, TX 77507

☐ *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section II

☒ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of an amendment to add label language to reduce the potential for product misuse.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☒ Yes* ☐ No	☒ Yes ☐ No	☐ Yes ☒ No	☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag
**Certification must be submitted*	If "Yes" Unit Packaging wgt. 0.023 fl oz (0.67 ml) 0.045 fl oz (1.34 ml) 0.091 fl oz (2.68 ml) 0.136 fl oz (4.02 ml) — No. per Container 1, 2, 3, 4, 5, 6, 12, 24 vials	If "Yes" Package wgt. — No. per Container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	0.023 fl oz (0.67 ml), 0.045fl oz (1.34 ml), 0.091 fl oz (2.68 ml), 0.136 fl oz (4.02 ml)	☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☒ Other _____ ☐ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Anne Turnbough	Director, Regulatory Affairs	281-892-2532

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature BY: Anne M Turnbough	3. Title Director, Regulatory Affairs
4. Typed Name: Anne Turnbough	5. Date: 8/30/2013

Material Sent for Data Extraction

Reg # 53883-312

Description: New Registration

☒ Material(s) Sent to Data Extraction Contractors:

- ☒ New Stamped Label Dated 6/28/13
- ☐ Notification Dated _____
- ☐ New CSF(s) Dated _____
- ☐ Other: _____

☒ Decision #: 46591

☐ Other Action/Comments: _____

Attach this coversheet to the top of the material or jacket. It must be well organized and clipped together, NOT STAPLED. Then give the material with this coversheet to staff in the Information Services Center (Room S-4900).

Reviewer: Kent Bellows John Hebert

Phone: 308-6249. Division: RD - IRB

Date: _____

Created February 3, 2011

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505C)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:
_X_ Registration
___ Reregistration
(under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
53883-312	JUN 28 2013

Term of Issuance:
Conditional

Name of Pesticide Product:
CSI Fipronil + Novaluron Spot-On for dogs

Name and Address of Registrant (include ZIP Code):
Control Solutions, Inc.
5903 Genoa-Red Bluff Road
Pasadena, TX 77507

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(B) provided that you:

1. Submit and/or cite all data required for registration/registration review of your product under FIFRA when the Agency requires all registrants of similar products to submit such data. You must comply with DCI ID# GDCI-129121-1305 issued on 3/14/2013. If you have questions about the Generic DCI issued, you may contact Susan Bartow from the Pesticide Re-evaluation Division.

2. Make the following label changes before you release the product for shipment:

   - Revise the EPA Registration Number to read, "EPA Reg. No. 53883-312."

Signature of Approving Official:

John Hebert, Product Manager 07
Insecticide-Rodenticide Branch, Registration Division (7505P)

Date: June 28, 2013

EPA Form 8570-6

3. Submit Storage stability (830.6317) and corrosion characteristics (830.6320) data within 18 months from the date of this registration notice.

4. Submit one copy of the revised print-ready/marketed final printed label (as defined in 40 CFR 152.3) containing all graphics, colors, font sizes, marketing claims, etc. The label must be accepted by the Agency prior to sale and distribution.

Other Conditions:

This registration is time-limited and expires two years from the date this product is first released for shipment.

A. You must provide the Agency with a projected release for shipment date within 30 days of the date of this Notice of Registration. The Agency will calculate the expiration date based on the projected release for shipment date until an actual release for shipment date is provided in writing.

B. Consider limiting the formulations of each product to one basic confidential statement of formula. The Agency may require this in the future. It is possible that no additional alternate formulations or minor formulation amendments will be approved for this product in the future.

C. You must submit quarterly enhanced incident reports and quarterly sales information in doses sold for this product for the quarter that begins on *October 1, 2013.*

The quarterly reports are due two months after each quarter ends. Please flag any Confidential Business Information as such. Enhanced incident reporting should be submitted to the Product Manager. Quarterly sales information should be submitted to the Pesticide Re-evaluation Division (7504P), Immediate Office (attn: Ms. Kaitlin Keller).

The following is a list of information that must be included in the quarterly reports for each incident:

EPA Registration Number
Product name (brand name)
Lot #
Where purchased: internet, store, veterinarian
Active Ingredient(s)
Weight range for product

Date on which incident occurred. (mm/dd/yyyy)
State in which the incident occurred. (standard 2 letter abbreviation)
Registrant case #

Species: dog, cat, other (specify)
Breed: (as reported by pet owner)
Age: months or years
Sex: M, F, or neutered
Weight: pounds

Primary Route of Exposure: dermal, oral, other animal, inhalation, other
Body System: neurological, dermatological, GI, respiratory, ocular, other
Major signs noted with separate column for each sign, using standard terminology
Time to Onset: (hours, days)
Treated by veterinarian: yes or no
First time product used: yes or no
Misuse: use on incorrect species, overdose, too frequent dosing, other (describe)
Any known precondition
EPA Severity Code: death, major, moderate, minor
Outcome: died, recovered, still treated, unknown

D. Along with the enhanced incident reporting, you must submit an analysis of the incidents seen, to include the following details:

- All incidents should be reported including all minor dermal and ocular irritation reports.

- Summary table for cats showing number of incidents of each severity code for each route of exposure. Each incident should only be reported once. If one incident has several routes of exposure, the order should be ocular > oral > dermal. In other words, an incident with both oral and dermal exposure would be reported as oral exposure, and an incident with both ocular and oral exposure would be reported as ocular exposure.

- A similar summary table for dogs (misuse or secondary exposure) showing number of incidents of each severity code for each route of exposure.
- Summary table for dogs and table for cats showing number of incidents that are believed due to secondary exposure (e.g., multi-pet households).
- A summary table for cats showing number of incidents for each severity code for these age ranges: <3 months, 3-6 months, 6-9 months, 9-12 months, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7 yr, 8 yr, 9 yr, 10 yr, 11 yr, 12 yr, 13 yr, 14 yr, 15 yr, >15 yr.
- A summary table showing the number of cat incidents for each severity code for each pet weight range on the product label (if applicable).
- A summary table for cat weight showing number of incidents for each product weight range. This table should show number of incidents in cats weighing less than that product weight range, number of incidents in cats in lower half of weight range, number of incidents in cats in upper half of weight range, and cats weighing more than the product weight range (if applicable).
- Table showing number of incidents for each cat breed, where provided.
- Table showing number of incidents in cats for each clinical sign.
- Table showing number of incidents in cats for each organ system.
- Report aggregate incidents, but do not combine moderate and minor incidents.

If the Agency determines that future mitigation measures are necessary for all pet spot-on products, you will be informed, and be expected to comply. If mitigation measures are necessary, the Agency may take appropriate regulatory actions.

Please note that, should you wish to add/retain a reference to the company's website on your label, the website then becomes labeling under the Federal Insecticide Fungicide and Rodenticide Act and is subject to review by the Agency. If the website is false or misleading, the product would be misbranded and unlawful to sell or distribute under FIFRA section 12(a)(1)(E). 40 CFR 156.10(a)(5) list examples of statements EPA may consider false or misleading. In addition, regardless of whether a website is referenced on your product's label, claims made on the website may not substantially differ from those claims approved through the registration process. Therefore should the Agency find or if it is brought to our attention that a website contains false or misleading statements or claims substantially differing from the EPA approved registration, the website will be referred to the EPA's Office of Enforcement and Compliance Assurance.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. If you have any questions, please contact Autumn Metzger at 703-305-5314 or metzger.autumn@epa.gov.

A stamped copy of the label is enclosed for your records.

John Hebert
Product Manager07
Insecticide-Rodenticide Branch
Registration Division (7505P)

Enclosure

{FRONT LABEL}

CSI Fipronil + Novaluron Spot-On for Dogs

[For use only on dogs 8 weeks of age or older]
[For use only on dogs 8 weeks old and older]
[For use only on dogs more than 8 weeks old]
[For use only on dogs [&][and] puppies 8 weeks or older and 6.5/6½ lbs. and over]
[For use only on dogs 6.5/6½ lbs. and over [and][&] over 8 weeks of age]
[Only apply to puppies over 8 weeks old]
[Only apply to puppies 8 weeks or older]
[Apply to dogs 8 weeks of age or older]
[Apply only to dogs 8 weeks of age or older]
[Apply to dogs >8 weeks old]
[Apply only on dogs [and puppies] [>6.5/6½ lbs./more than 6.5/6½ lbs. [and/&] over 8 weeks old]

{One of following will be used on label}
[For use ONLY on dogs [&][and] puppies]
[ONLY for Dogs & Puppies 8 weeks or older [and][&] 6.5/6½[-] [to] 22 lbs]
[6.5/6½[-] [to] 22 lbs] [Only for Dogs 6.5/6½[-] [to] 22 lbs.]
[23[-] [to] 44 lbs] [Only for Dogs 23[-] [to] 44 lbs.]
[45[-] [to] 88 lbs] [Only for Dogs 45[-] [to] 88 lbs.]
[89[-] [to] 132 lbs] [Only for Dogs 89[-] [to] 132 lbs.]
[over 8 weeks of age]]
{or}
[Only for Dogs 6.5/6½-22 lbs. & Puppies (8 weeks or older)]
[Only for Dogs 23-44 lbs.]
[Only for Dogs 45-88 lbs.]
[Only for Dogs 89-132 lbs.]

ACCEPTED
JUN 28 2013
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide Registered under EPA Reg. No. 53883-312

ACTIVE INGREDIENTS:

Fipronil	9.8%
Novaluron	20.0%
OTHER INGREDIENTS:	70.2%
TOTAL:	100.0%

{1.5 cm x 1.5 cm or as listed below/bottom right corner of front panel}

KEEP OUT OF REACH OF CHILDREN
CAUTION

[See [Back][or][Side] [Label[s]] [Panel[s]] [or] [insert] for Additional Precautionary Statements]

{Option 1: Net Contents related to specific CRP packaging}
NET CONTENTS: X fl oz [Y – X fl oz applicators]
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][Twenty-Four] 0.023 fl oz (0.67 mL) applicators
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][TwentyFour] 0.045 fl oz (1.34 mL) applicators
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][Twenty-Four] 0.091 fl oz (2.68 mL) applicators
[1][One][2][Two][3][Three][4][Four][5][Five][6][Six][12][Twelve][24][Twenty-Four] 0.136 fl oz (4.02 mL) applicators
{End Option 1}

{Option 2: Net Contents related to specific CRP packaging}
NET CONTENTS: X fl oz [3 – X fl oz applicators]
[[Three] [3] 0.023 fl. oz. (0.67 mL) applicators]
[[Three] [3] 0.045 fl. oz. (1.34 mL) applicators]
[[Three] [3] 0.091 fl. oz. (2.68 mL) applicators]
[[Three] [3] 0.136 fl. oz. (4.02 mL) applicators]
{End Option 2}

{Front label may include various marketing statements, refer to Optional Marketing Language section}

{END FRONT LABEL}

{BACK LABEL}

READ ENTIRE LABEL BEFORE EACH USE.
USE ONLY ON DOGS AND PUPPIES OVER 8 WEEKS OF AGE.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS. CAUTION: Harmful if swallowed. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

FIRST AID	
If swallowed	• Immediately call a poison control center or doctor. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Have person sip a glass of water if able to do so. • Do not give anything by mouth to an unconscious person.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment. [You may also contact [XXX-XXX-XXXX] for emergency medical treatment information.]

HAZARDS TO DOMESTIC ANIMALS. For external use on dogs only. Individual sensitivities, while rare, may occur after using any pesticide product on dogs. If signs of sensitivity occur bathe your dog with a mild soap and rinse with large amounts of water. If signs persist, or become more severe within a few days of application, consult a veterinarian immediately. If your dog has an unusual reaction to the initial application, consult a veterinarian before repeating treatment. Certain medications can interact with pesticides. Consult a veterinarian before using on medicated, known organ dysfunction, debilitated or aged dogs. [Call [XXX-XXX-XXXX] for 24-hour assistance.]

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. DO NOT ALLOW CHILDREN TO APPLY PRODUCT. TO PREVENT HARM TO YOU AND YOUR DOG, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. Do not have contact or allow children contact with treated area until completely dry.

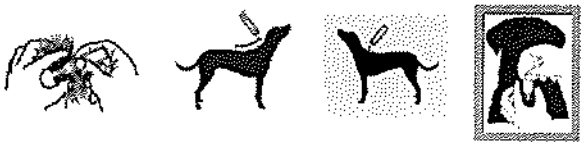
Do not use on puppies under 6.5/6½ pounds and 8 weeks of age. Do not allow your dog to ingest this product. Use entire contents of tube on each dog. Do not split one tube between dogs. Do not use multiple tubes on one dog. Weigh your dog to be sure you are applying the right dose formulated for the weight of your dog. Do not treat your dog with more than one pesticide product at a time. Do not use on rabbits or animals other than dogs. Do not use on pregnant or lactating dogs. Separate the treated dog from all other dogs and cats for 24 hours after treatment has been applied.

Side Effects: Monitor your dog after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Individual sensitivities, while rare, may occur after using any pesticide product. If signs persist, or become more severe within a few days of application, consult a veterinarian immediately. If your dog has an unusual reaction to the initial application, consult a veterinarian before repeating treatment. Certain medications can interact with pesticides. [Call [XXX-XXX-XXXX] for 24-hour assistance.]

DO NOT USE ON CATS. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.

{1.5 cm x 1.5 cm or as listed below/bottom right corner of back panel}

[Optional drawings that may or may not appear anywhere on finished label]



[[Application Instructions] [How to Apply - May contain graphics illustrating product use, e.g., dog with a drop falling onto its neck from a vial on front, side, or back carton label and/or applicator labeling.]

Only For Dogs Weighing 6.5/6½[-][to]22 lbs. [including small dogs and puppies,] 8 weeks or older
[For cartons containing 0.023 fl. oz. (0.67 ml) applicator tubes]
Apply one [tube] [applicator] (0.023 fl. oz.) (0.67 ml) [as a spot [on][to] the dog's back between the shoulder blades][from the back of the neck to a point midway between the neck and tail].

Only for Dogs Weighing Between 23[-][to]44 lbs.
[For cartons containing 0.045 fl. oz. (1.34 ml) applicator tubes]
Apply one [tube] [applicator] (0.045 fl. oz.) (1.34 ml) [as a spot [on][to] the dog's back between the shoulder blades] [from the back of the neck to a point midway between the neck and tail].

Only for Dogs Weighing Between 45[-][to]88 lbs.
[For cartons containing 0.091 fl. oz. (2.68 ml) applicator tubes]
Apply one [tube] [applicator] (0.091 fl. oz.) (2.68 ml) [as a spot[on][to] the dog's back between the shoulder blades] [from the back of the neck to a point midway between the neck and tail].

Only for Dogs Weighing 89[-][to]132 lbs.
[For cartons containing 0.136 fl. oz (4.02 ml.) applicator tubes]
Apply one [tube] [applicator] (0.136 fl. oz.) (4.02 ml) [as a spot [on][to] the dog's back between the shoulder blades] [from the back of the neck to a point midway between the neck and tail].
Do not use two tubes on dogs greater than 132 lbs.

FREQUENCY OF APPLICATION
Use [Brand Name] monthly for control of flea, tick, flea egg, [and] chewing lice [and mosquito] infestations. [Studies show that] [Brand Name] kills adult fleas for up to three months. Apply monthly if your dog is at high risk for flea reinfestation[, or in a highly infested environment]. [Apply monthly to kill mosquitoes within 24 hours.] Apply monthly to control ticks[,] [mosquitoes] and chewing lice. Do not reapply for [30 days][4 weeks].

[If you have questions or comments about this product, please write: CSI Consumer Response, 5903 Genoa-Red Bluff Road, Pasadena, TX 77507]

[In Case of Emergency, call: XXX-XXX-XXXX]
[For more information]
[Non-Emergency, call XXX-XXX-XXXX]
[Made in USA]

[Distributed by:][Manufactured by:]
Control Solutions, Inc.
5903 Genoa-Red Bluff Road
Pasadena, TX 77507

EPA Reg. No. 53883-GRE
EPA Est. No. XXXXX-XX-XXX

{END BACK LABEL}

{FOLLOWING TEXT MAYBE FOUND ON SIDE PANELS, BACK PANEL AS SPACE PROVIDES OR PRODUCT INSERT}

{Option 1: How to open label language related to specific CRP packaging}
[Option 1a]
How to open: Remove product tube[s] [vial] from the package. [Separate one tube from the others.] Hold the tube [vial] with notched end pointing up and away from the face and body of you and your dog. Use scissors to cut off the narrow end at the notches along the line.

How to apply: Invert tube over dog and use open end to part dog's hair. Squeeze tube firmly to apply all of the solution to the dog's skin, as directed below. [Do not apply more often than once every 4 weeks.] [Repeat application may be made if necessary, but do not apply more often than once every 30 days.] [Repeat application [may][can] be made every four weeks.]

[Option 1b]
How to open

1. Remove product tube[s] [vial] from the package.
2. [Separate one tube from the others.] Hold the tube [vial] with notched end pointing up and away from the face and body of you and your dog. Use scissors to cut off the narrow end at the notches along the line.

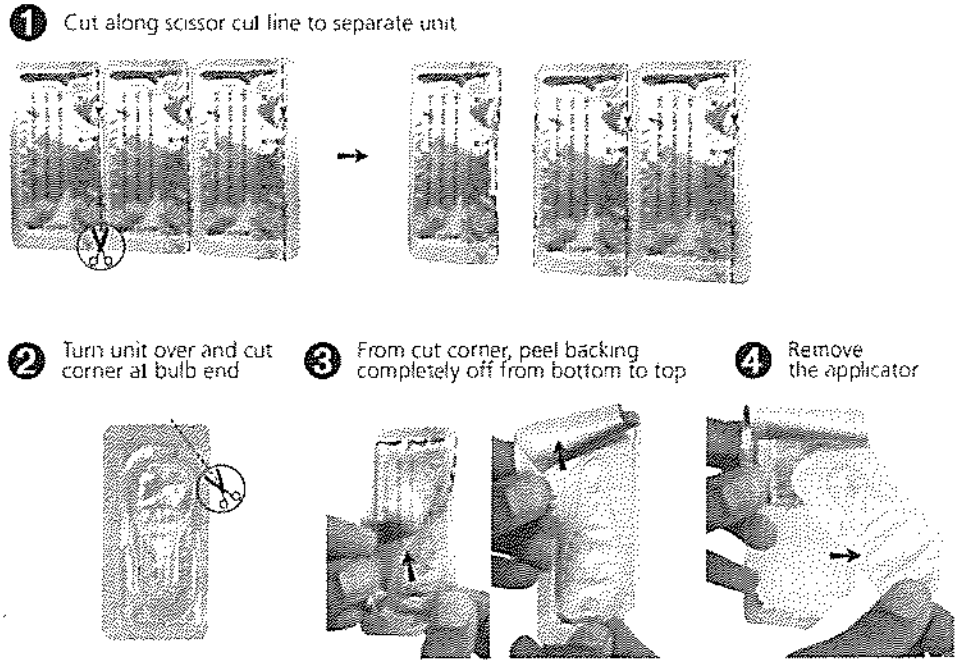
How to apply

1. Invert tube over dog and use open end to part dog's hair.
2. Squeeze tube firmly to apply all of the solution to the dog's skin [as a spot [on][to] the dog's back between the shoulder blades.] [or] [from the back of the neck to a point midway between the neck and tail.]

{End Option 1}

{Option 2: How to open label language related to specific CRP packaging}

DIRECTIONS FOR OPENING PACKAGING:



{End Option 2}

[Brand Name] contains fipronil and the insect growth regulator (IGR) novaluron. [Brand Name] effectively targets fleas and ticks. [Brand Name] features a sustained release formula created to act fast and provide [long lasting] control of fleas, ticks, flea eggs, [mosquitoes] and chewing lice for up to [1 month] [[four] [4] weeks] [30 days]] on dogs.

STORAGE AND DISPOSAL

PESTICIDE STORAGE: Do not remove tube from the pack until ready to use. Store in a cool [below 77°F[/] (25°C)] dry place inaccessible to children and pets. Do not refrigerate. Protect from direct sunlight.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: If empty: Non-refillable container. Do not reuse or refill this container. Offer for recycling if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

[LIMITATION OF WARRANTY AND LIABILITY

Read the entire direction for use, conditions of warranties and limitations of liability before using this product. If terms are not acceptable, return the unopened product container at once. By using

this product, user or buyer accepts the following **CONDITIONS, DISCLAIMER OF WARRANTIES**, and **LIMITATIONS OF LIABILITY**.

CONDITIONS: The directions for use of this product are believed to be adequate and must be followed carefully. However, it is impossible to eliminate all risk associated with the use of this product. Animal injury, ineffectiveness or other unintended consequences may result because of such factors as presence of other materials, or the manner of use or application, all of which are beyond the control of Control Solutions, Inc. To the extent consistent with applicable law, all such risks shall be assumed by the user or buyer.

DISCLAIMER OF WARRANTIES: To the extent consistent with applicable law, Control Solutions, Inc. makes no other warranties, express or implied, of merchantability or of fitness for a particular purpose or otherwise, that extend beyond the statements made on this label. No agent of Control Solutions, Inc. is authorized to make any warranties beyond those contained herein or to modify the warranties contained herein. To the extent consistent with applicable law, Control Solutions, Inc. disclaims any liability whatsoever for special, incidental or consequential damages resulting from the use or handling of this product.

LIMITATIONS OF LIABILITY: To the extent consistent with applicable law, the exclusive remedy of the user or buyer for any and all losses, injuries or damages resulting from the use or handling of this product, whether in contract, warranty, tort, negligence, strict liability or otherwise, shall not exceed the purchase price paid or at Control Solutions, Inc. election, the replacement of product.]

[If you have questions or comments about this product, please write: CSI Consumer Response, 5903 Genoa-Red Bluff Road, Pasadena, TX 77507]

[In Case of Emergency, call: XXX-XXX-XXXX]
[For more information]
[Non-Emergency, call XXX-XXX-XXXX]
[Made in USA]

[Distributed by:][Manufactured by:]
Control Solutions, Inc.
5903 Genoa-Red Bluff Road
Pasadena, TX 77507

EPA Reg. No. 53883-GRE
EPA Est. No. XXXXX-XX-XXX

[Look at the Label [Look at the Label icon] 6 Step [Spot-On] [Squeeze-On] [Topical] Checklist

- Read the label completely and follow directions
- Weigh your dog
- Do NOT use Dog products on Cats

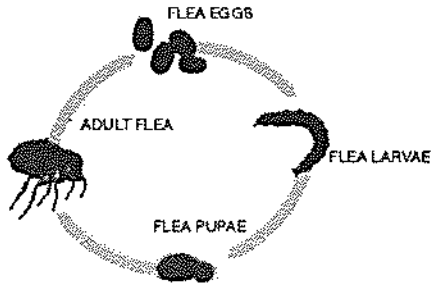
- Do NOT treat with more than one pesticide product at a time
- Separate animals after treatment for at least 24 hours to avoid chance of ingestion
- Do NOT split tubes between Dogs [and use the ENTIRE tube contents].]

[**Brand Name**]
[1][2][3][4][5][6][12][24] [Month [Treatment] [Application] Tracker]
[Monthly reminder card]
[Apply [Brand Name] monthly for continuous protection against fleas, ticks, flea eggs [and] chewing lice [and mosquitoes].]
[For year-round protection, apply [Brand Name] monthly.]
[Pet's Name (Empty blank for owner to fill in name)]
[First][1st][Second][2nd][Third][3rd][Fourth][4th][Fifth][5th][Sixth][6th][Seventh][7th][Eighth][8th][Ninth][9th][Tenth][10th][Eleventh][11th][Twelfth][12th]
[Dose] [Treatment] [Application]
[(Empty blank for owner to fill in date)(Date: MM/DD/YY)]
[Calendar stickers with brand name] [Place stickers on your calendar as a reminder to reapply [brand name] in 30 days.]

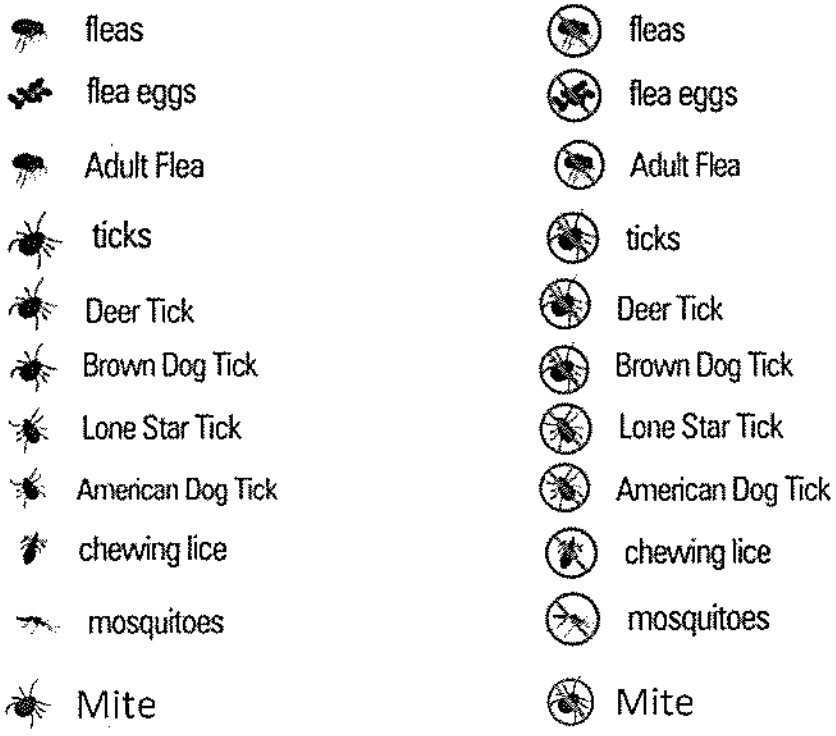
[Monthly Application Reminder Magnet]
[Enclosed for your convenience is an application reminder magnet. Push the (reset) button to start the clock. After 30 days the magnet will flash (and beep) reminding you to reapply [Brand Name]. This application reminder can be used for future treatments. Just press the reset button and in another 30 days the reminder magnet will flash (and beep) reminding you to reapply.]

{END: TEXT THAT MAYBE FOUND ON SIDE PANELS, BACK PANEL AS SPACE PROVIDES OR PRODUCT INSERT}

{Optional graphics below may or may not appear anywhere on finished label}



[Flea life cycle diagram] [Flea Life Cycle]
[Sample coloring and layout may be different on final label]



{End optional graphics}

{TUBE / VIAL LABEL}

{Option 1 Tube label related to CRP Option 1}

Front Label	Back Label
Brand Name {cat graphic with line through it} **Use only on dogs 8 weeks and older and [6.5/6½-22][23-44][45-88][89-132] lbs.** Fipronil 9.8%, Novaluron 20.0% w/w [0.023 fl oz **(or)** 0.045 fl oz **(or)** 0.091 fl oz **(or)** 0.136 fl oz] [label code]	KEEP OUT OF REACH OF CHILDREN CAUTION: Read directions and precautions before using. Use scissors to open. EPA REG. No. 53883-GRE [label code]

{End Option 1}

{Option 2 Blister pack label related to CRP Option 2}

{START – BLISTER PACK INFORMATION}

{END – BLISTER PACK INFORMATION}

Front Label	Back Label
Brand Name {cat graphic with line through it} **Use only** on **dogs 8 weeks and older and [6.5/6½-22][23-44][45-88][89-132] lbs.** Fipronil 9.8%, Novaluron 20.0% w/w [0.023 fl oz **(or)** 0.045 fl oz **(or)** 0.091 fl oz **(or)** 0.136 fl oz] [label code]	KEEP OUT OF REACH OF CHILDREN CAUTION: Read directions and precautions before using. EPA REG. No. 53883-GRE [label code]

{End Option 2}

{OPTIONAL MARKETING LANGUAGE THAT MAY BE FOUND ON ANY PANEL OR INSERT OF THE LABEL OR PACKAGING}

[**Fleas**]
[• Research demonstrates that [brand name] kills adult fleas and flea eggs for up to one month]
[• [Brand Name] prevents development of fleas for up to one month]
[• Prevents adult fleas and flea eggs]
[• If dog is a high risk for flea reinfestation, a once a month application is needed]
[• Kills flea eggs for up to 1 month]
[• With Novaluron Insect Growth Regulator which Breaks the Flea Life Cycle]
[• With Novaluron to Break Flea Life Cycle]
[• With Insect Growth Regulator to Break Flea Life Cycle]
[• Dual Action [!]:Fipronil with Novaluron IGR Effectively Breaks the Flea Life Cycle]
[• Dual Action [!]: Effectively Breaks the Flea Life Cycle[!]]
[• Kills Fleas Up to [4 weeks][1 month][30 days]!]
[• Prevents Flea Eggs From Developing Into Biting Adults]
[• Breaks the flea life cycle]
[• Effectively kills adult fleas and flea eggs]
[• Kills adult fleas [for up to three months]]
[• Kills newly emerged adult fleas before they lay eggs]
[• Kills adult fleas, which may cause [flea allergy dermatitis] [and][or] [flea bite anemia]]
[• Kills Fleas]
[• Kills Flea Eggs]

[**Ticks**]
[• Kills Ticks]
[• Kills ticks including those that may transmit Lyme disease]
[• Kills Ticks for Up to [4 weeks][1 month][30 days]!]*
[• Kills [all stages of] deer ticks [(which may be a vector of Lyme disease)][(including those that may transmit Lyme disease)] for up to [4 weeks][1 month][30 days]]
[• Kills all stages of deer ticks]
[• Kills Ticks (including deer ticks) for up to [4 weeks][1 month][30 days]]
[• Kills [brown [dog ticks],] [American [dog ticks],] [and] lone star [ticks]] [dog ticks] [and] [deer ticks] [(*Rhipicephalus sanguineus*)] [for up to [4 weeks] [1 month][30 days]]]
[• Kills American dog ticks [(*Dermacentor variabilis*)] for up to [4 weeks][1 month][30 days!]
[• Kills ticks that may transmit Lyme disease, Rocky Mountain spotted fever, ehrlichiosis, babesiosis, and anaplasmosis]

[**Mosquitoes**]
[• Kills mosquitoes] [within 24 hours for up to 7 days] [and] [within 48 hours for up to 28 days]

[**Multiple Pests**]
[• Flea & Tick Control for Dogs & Puppies 8 weeks old and older]
[• Kills fleas, flea eggs, ticks, chewing lice [& mosquitoes][for up to 4 weeks][30 days]1 month]]
[• Controls flea reinfestation for up to [4 weeks][four weeks][one month]]
[• Kills fleas, ticks, [mosquitoes,] chewing lice and flea eggs][for up to] [1 month][30 days][4 weeks]]
[• Monthly flea, tick, [mosquito], chewing lice, and flea egg protection]
[• Monthly flea, tick, [mosquito] and chewing lice protection]
[• Kills fleas, ticks, [mosquitoes], flea eggs and chewing lice]
[• [Six] [6] [5][Five] Way Protection [Kills fleas, ticks, [mosquitoes], [mites], chewing lice and flea eggs]]
[• [5] [Five] [Four][4] Way Protection! Kills fleas, ticks, [mosquitoes], chewing lice, [and] [&] flea eggs]
[• [4 Week] [1 month][30 day][Flea and Tick [Treatment][Application]]
[• [Four (4) Week] [Flea, Tick, [Mosquito,] [flea egg,] and chewing lice control]
[• 4 week Flea and Tick Treatment!]
[• Once A Month Flea and Tick [Treatment][Application]]
[• Kills Fleas and Ticks for up to 4 weeks!]
[• When used monthly [brand name] completely breaks the flea life cycle and controls tick and chewing lice infestations.]
[• Use [Brand Name] monthly to control fleas, ticks, [mosquitoes], flea eggs [and chewing lice]]
[• Kills Fleas, Ticks & Flea Eggs for up to 4 Weeks]

[**Other**]
[• Only for Dogs and Puppies 8 weeks of age or older]
[• Can only be used on puppies 8 weeks of age and older]
[• Formulated for Dogs and Puppies 8 weeks of age or older]
[• Only for Dogs [6.5/6½-22 lbs], [23-44 lbs], [45-88 lbs], [89-132 lbs]
[• Fast Acting]
[• Long Lasting]
[• Once a month treatment]
[• Convenient and simple spot treatment]
[• Convenient spot treatment]
[• A once monthly application is required for chewing lice]
[• Rapidly eliminates infestations of chewing lice]
[• Rapid elimination of chewing lice infestation[s]]
[• Kills chewing lice][and aids in the control of mites that may cause sarcoptic mange]
[• Aids in Control of Sarcoptic Mange]
[• Controls mites that cause sarcoptic mange]
[• [X] Applications {for cartons with [X] applicators}] and/or [[X] Month Supply] or [[X] Week Supply]
[• Best if used year round!]

[• For year-round protection, apply [Brand Name] monthly]
[• (ICON Showing 4 Week Protection)]
[• 4 Week Dose!]
[• 1 Month Dose!]
[• 30 Day Dose!]
[• Easy to Use [Application]]
[• Formulated for Dogs and Puppies over 8 weeks of age]
[• Patented Technology]
[• Apply once every [4 weeks][month][30 days]!]
[• Repeat application [may][can] be made every four weeks.]
[• Apply monthly]
[• Fipronil (9.8%) + Novaluron (20.0%)]
[• Prevents and controls reinfestation[s] of listed pests [for 4 weeks] [for 1 month][for 30 days]]
[• Stops existing infestations of listed pests]
[• Prevents [establishment of additional infestation] [infestation of listed pests] [for] [1 month][4 weeks][30 days]]
[• Lift here for more information]
[• [One Application][Two Applications][Three Applications][Four Applications][Five Applications][Six Applications][Twelve Applications][Twenty-Four Applications] and/or [1 Month Supply][2 Month Supply][3 Month Supply][4 Month Supply][5Month Supply][6 Month Supply][12 Month Supply][24 Month Supply] or [4 Week Supply][8 Week Supply][12 Week Supply][16 Week Supply][Twenty Week Supply][24 Week Supply][48 Week Supply][52 Week Supply][104 Week Supply]]
[• [1][2][3][4][5][6][12][24] Applications]
[• Contains Fipronil[,] [-]the [same] active ingredient used in Frontline® brand products*]
[• Contains Fipronil[,] [-]the [same] active ingredient used in the leading competitive brand[s]]
[• *[Brand Name] is not manufactured by or distributed by Merial. Frontline® is a registered trademark of Merial.]
[• [Brand Name] is a trademark of [**Company Name**]]

Hebert, John

From: Metzger, Autumn
Sent: Tuesday, June 18, 2013 9:39 PM
To: James Messina
Cc: Anne Turnbough (aturnbough@ControlSolutionsInc.com); Hebert, John; Terry McNamara
Subject: RE: CSI Pending Action

Hi James,

After consultation with the PERC (efficacy review team), it has been decided that the rationale for the control issue was not strong enough as we have seen other studies showing much better control results. The current efficacy review and its recommendations still stands, with the exception of the few points we okayed in a later email.

Please go ahead and make all necessary revisions to the label and have back to me by the end of this week so we can ensure completion by the PRIA date, which is next Friday.

Thanks for all the supporting materials and discussions.
Autumn

From: James Messina [mailto:jmessina@exponent.com]
Sent: Thursday, June 13, 2013 11:34 AM
To: Metzger, Autumn
Cc: Anne Turnbough (aturnbough@ControlSolutionsInc.com); Hebert, John; Terry McNamara
Subject: RE: CSI Pending Action

Dear Autumn,

Thanks for the update. I am actually glad to hear you were able to enjoy your vacation. These days it is a hard thing to do with all of the technology.

Please let us know when you receive feedback from the PERC team on the efficacy part.

We reviewed EPA's response below related to the minimum weight based upon the submitted CASS data, and we are a bit confused with TRB's response. Study MRID 48843210 meets the OCSPP guideline requirements (870.7200) for the CASS testing, and has been reviewed and accepted to support use on dogs and puppies 8 weeks of age and older. This study does have 6 puppies per dose group, and not 10, nor 12, nor 14, etc., so taking the mean from the lowest weight 4 females and 4 males is not possible. Previously the minimum weight was recommended as 7 lbs based upon the mean weight of all six SX puppies being 6.26 lbs, which was then rounded up to 7 lbs. As previously related, because the study demonstrated a safety margin of at least SX with puppies having a mean weight of 6.26 lb, there is no need nor reason to round up to 7 lbs. At a minimum we believe that the low weight should be 6.3 pounds (no rounding as there is sufficient conservatism in the Sx data). If the Agency believes it has to round the minimum weight then we believe it should be 6.S pounds. We are aware of several spot-on labels that have ½ pound increments on the EPA stamp approved label.

We welcome the opportunity to discuss this issue with you or Byron. Please let us know who is the best person to contact to discuss it in more detail. Many thanks.

Best Regards,

James Messina

Exponent
202.772.4932 office
301.908.1181 mobile

From: Metzger, Autumn [mailto:Metzger.Autumn@epa.gov]
Sent: Tuesday, June 11, 2013 3:34 PM
To: James Messina
Cc: Anne Turnbough (aturnbough@ControlSolutionsInc.com); Hebert, John
Subject: RE: CSI Pending Action

Hi James,

I did not end up having access to my email last week, but that made not working during my vacation easier ☺. The PERC team is still reviewing the efficacy portion but Iw will work on it so we can know soon and move forward.

As for the minimum weight question, the response from TRB is that MRID 48843210 utilized only 6 (3M & 3F) puppies per dosage group. We could reconsider if there were 10 or more puppies/group (taking the mean of the 4 least weight males and 4 least weight females in the 5X group), but this isn't the situation here.

Autumn

From: James Messina [mailto:jmessina@exponent.com]
Sent: Monday, June 10, 2013 3:34 PM
To: Metzger, Autumn
Cc: Anne Turnbough (aturnbough@ControlSolutionsInc.com)
Subject: CSI Pending Action

Autumn,

I wanted to check-in with you to see if the Agency has any questions on the information we submitted on the CSI Fipronil + Novaluron Spot-on for Dogs pending application? Our understanding is that we are holding with any additional label revisions until we hear back from you. Can you please confirm?

Many thanks.

Best Regards,

James Messina
Principal Regulatory Consultant
Exponent
Center for Chemical Regulation and Food Safety
1150 Connecticut Avenue, N.W.
Suite 1100
Washington, DC 20036
202-772-4932
202-772-4979 fax
301-908-1181 cell

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

April 16, 2013

MEMORANDUM:

Subject:	Name of Pesticide Product:	CSI FIPRONIL + NOVALURON SPOT-ON FOR DOGS
	EPA Reg. No. /File Symbol:	53883-GRE
	DP Barcode:	DP 404003
	Decision No.:	465891
	Action Code:	R260
	PC Codes:	124002 (Novaluron: 20%) 129121 (Fipronil: 9.8%)

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505P)

Byron T. Backus
April 16, 2013
V. Hasley Team Leader/TCX

To: Autumn Metzger/John Hebert RM 07
Insecticide-Rodenticide Branch
Registration Division (7505P)

Registrant: CONTROL SOLUTIONS, INC.

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
129121 Fipronil	9.8%
124002 Novaluron	20.0%
Other Ingredients:	70.2%
TOTAL	100.0%

ACTION REQUESTED: "This product is a new spot-on with the combination of Fipronil + Novaluron. This is a new use for Novaluron (as far as spot-ons are concerned)... With this application I have enclosed: the cover letter with transmittal sheet, the data matrix (your studies highlighted)..."

BACKGROUND: The material received by TRB includes a cover letter (dated June 6, 2012), five CSFs (one basic, four alternate, all dated June 6, 2012), a label, a data matrix (which indicates a new companion animal animal safety study – in MRID 48843210 – has been submitted in addition to citations – MRIDs 43121110, 43121111, 43444905, 43577711 and 43863802 – to previously submitted studies).

COMMENTS AND RECOMMENDATIONS:

1. The primary review for the companion animal safety study in MRID 48843210 (adult dogs and puppies) was conducted by TRB.

2. The following is the executive summary for the study in MRID 48843210:

   In a companion animal safety study (MRID 48843210), groups consisting of three 8-week-old (±1 day) puppies and three adult (>10 months old) beagles/sex (total of 12 dogs/group) were treated on Day 0 with either three 1X applications of formulation (Group A): five 1X applications of formulation (Group B) or five 1X applications of placebo control substance (Group C). A 1X application of formulation consisted of 0.67 mL for dogs weighing ≤ 10 kg and 1.34 mL for dogs >10 kg. A 1X application of placebo control was 0.47 mL for dogs ≤ 10 kg and 0.94 mL for dogs >10 kg [although not stated in the report, it was confirmed on April 9, 2013 by the registrant's representative that ECS-28-99-2 is the formulated product minus the active ingredients; this is consistent with dosage given as the nominal percentage of other ingredients is 70.2%, and 0.702 x 0.67 mL (for dogs = ≤ 10 kg) 0.47 mL and 0.702 x 1.34 mL (for dogs > 10 kg) = 0.94 mL]. Applications were spaced one hour apart.

   The test or placebo control material was applied directly to the skin on the dorsal midline from the base of the skull to the interscapular region. Dogs were treated on day 0 and observed through day 14.

   Puppies and adult dogs were observed twice daily (generally AM and PM). Post-application clinical observations included seizure activity in a Group A (3X) male puppy on day 11, described [p. 22 of MRID 48843210] as a "self-limited episode…that did not require medical intervention." Also from p. 22: "As this self-limited event occurred only once 11 days after treatment in a 3X puppy, and no other animals, including all the 5X animals did not experience this, it was judged to not be treatment-related." The only other mention of this event is in Table 3 on p. 72 of MRID 48843210, where the seizure [described as "moderate"] is reported for day 11. Other observations included gastrointestinal findings (primarily loose feces and diarrhea [including one incident of bloody diarrhea in a 5X control animal on day 11] with occasional incidents of vomiting), discharge from one or both eyes, irritation in one or both ears (occurring only in adults of all groups, appearing 4-5 days after treatment, often persisting through day 14), and flaking of the skin at the application site without underlying redness or other signs of inflammation.

There were no treatment-related effects on mortality, body weight, hematology, coagulation or clinical chemistry parameters. Mean group food consumption values for puppies were slightly lower on Day -1, possibly associated with the stress of being weighed. There was no indication of an effect on day 0 (day of application) or on subsequent days. For the adult dogs, group mean food consumption values were noticeably lower on day 0 (the day of application), and this was more pronounced in females but was consistent across all 3 groups. This may have been associated with the stress (excitement?) from the interaction with personnel during dosing, but in any case food consumption values returned to normal on day 1 so that even if this was considered to be an adverse effect it was transient.

We can accept the laboratory's conclusions regarding seizure activity in a Group A male puppy on day 11 as not being treatment-related. It is concluded that the margin of safety in adult and 8-week-old beagles administered Dog Spot-On ECS-28-99-1 is at least 5X the recommended dosing volumes of 0.67 mL for dogs and puppies ≤ 10 kg and 1.34 mL for dogs >10 kg and ≤ 20 kg. The study also supports dosages of 2.68 mL for dogs >20 kg and ≤ 40 kg, and 4.02 mL for dogs >40 kg and ≤ 60 kg. Since the mean weight of the 5X (Group B) puppies was 2.84 ± 0.28 kg (=6.26 ± 0.62 lbs) the data will support use on dogs and puppies (8 weeks and older) with a minimum weight of 7 lbs which must be declared on the label.

This companion animal safety study in adult dogs is **Acceptable** and **does satisfy** the guideline requirement for a companion animal safety study (OCSPP 870.7200) in adult dogs and puppies (weighing ≥7 lbs) with once-a-month treatment and dosage rates of 0.67 mL for 7-22 lbs, 1.34 mL for 23-44 lbs, 2.68 mL for 45-88 lbs, and 4.02 mL for 89-132 lbs.

EPA Primary Reviewer: Byron T. Backus, Ph.D.
Technical Review Branch, Registration Division (7505P)

Signature: Byron T. Backus
Date: April 16, 2013

EPA Secondary Reviewer: Masih Hashim, DVM
Technical Review Branch, Registration Division (7505P)

Signature: Hashim
Date: 4-16-13

Template version 02/06

DATA EVALUATION RECORD

STUDY TYPE: Companion Animal Safety Study - Adult and Juvenile Dogs; OCSPP 870.7200

PC CODES: 129121, 124002 **DP BARCODE:** 404003

TEST MATERIAL (PURITY): Dog Spot-On ECS-28-99-1; Lot No. ECS-28-99-1; Nominal composition: Fipronil 9.8%; Novaluron 20%; Analytical composition (average of 4 analyses): Fipronil 10.0%; Novaluron 20.6%. Described as a low viscosity clear liquid with a dull solvent odor.

SYNONYMS: CSI Fipronil + Novaluron Spot-On for Dogs

CITATIONS: Madsen, T. (2012) General Safety Evaluation of Fipronil-Novaluron Spot-On in 8-Week-Old Puppies and Adult Dogs: Final Report. Project Number: S11227/OCR. Unpublished study prepared by Sinclair Research Center, Inc. 142p. MRID 48843210.

SPONSOR: Control Solutions, Pasadena, TX

EXECUTIVE SUMMARY: In a companion animal safety study (MRID 48843210), groups consisting of three 8-week-old (±1 day) puppies and three adult (>10 months old) beagles/sex (total of 12 dogs/group) were treated on Day 0 with either three 1X applications of formulation (Group A); five 1X applications of formulation (Group B) or five 1X applications of placebo control substance (Group C). A 1X application of formulation consisted of 0.67 mL for dogs weighing ≤ 10 kg and 1.34 mL for dogs >10 kg. A 1X application of placebo control was 0.47 mL for dogs ≤ 10 kg and 0.94 mL for dogs >10 kg [although not stated in the report, it was confirmed on April 9, 2013 by the registrant's representative that ECS-28-99-2 is the formulated product minus the active ingredients; this is consistent with dosage given as the nominal percentage of other ingredients is 70.2%, and 0.702 x 0.67 mL (for dogs = ≤ 10 kg) 0.47 mL and 0.702 x 1.34 mL (for dogs > 10 kg) = 0.94 mL]. Applications were spaced one hour apart.

The test or placebo control material was applied directly to the skin on the dorsal midline from the base of the skull to the interscapular region. Dogs were treated on day 0 and observed through day 14.

Puppies and adult dogs were observed twice daily (generally AM and PM). Post-application clinical observations included seizure activity in a Group A (3X) male puppy on day 11, described [p. 22 of MRID 48843210] as a "self-limited episode...that did not require medical intervention." Also from p. 22: "As this self-limited event occurred only once 11 days after treatment in a 3X puppy, and no other animals, including all the 5X animals did not experience this, it was judged to not be treatment-related." The only other mention of this event is in Table 3 on p. 72 of MRID 48843210, where the seizure [described as "moderate"] is reported for day 11. Other observations included gastrointestinal findings (primarily loose feces and diarrhea [including one incident of bloody diarrhea in a 5X control animal on day 11] with occasional incidents of vomiting), discharge from one or both eyes, irritation in one or both ears (occurring only in adults of all groups, appearing 4-5 days after treatment, often persisting through day 14), and flaking of the skin at the application site without underlying redness or other signs of inflammation.

There were no treatment-related effects on mortality, body weight, hematology, coagulation or clinical chemistry parameters. Mean group food consumption values for puppies were slightly lower on Day -1, possibly associated with the stress of being weighed. There was no indication of an effect on day 0 (day of application) or on subsequent days. For the adult dogs, group mean food consumption values were noticeably lower on day 0 (the day of application), and this was more pronounced in females but was consistent across all 3 groups. This may have been associated with the stress (excitement?) from the interaction with personnel during dosing, but in any case food consumption values returned to normal on day 1 so that even if this was considered to be an adverse effect it was transient.

We can accept the laboratory's conclusions regarding seizure activity in a Group A male puppy on day 11 as not being treatment-related. It is concluded that the margin of safety in adult and 8-week-old beagles administered Dog Spot-On ECS-28-99-1 is at least 5X the recommended dosing volumes of 0.67 mL for dogs and puppies ≤ 10 kg and 1.34 mL for dogs >10 kg. ≤ 20 kg. The study also supports dosages of 2.68 mL for dogs >20 kg and ≤ 40 kg, and 4.02 mL for dogs >40 kg and ≤ 60 kg. Since the mean weight of the 5X (Group B) puppies was 2.84 ± 0.28 kg (=6.26 ± 0.62 lbs) the data will support use on dogs and puppies (8 weeks and older) with a minimum weight of 7 lbs which must be declared on the label.

This companion animal safety study in adult dogs is **Acceptable** and **does satisfy** the guideline requirement for a companion animal safety study (OCSPP 870.7200) in adult dogs and puppies (weighing ≥7 lbs) with once-a-month treatment and dosage rates of 0.67 mL for 7-22 lbs, 1.34 mL for 23-44 lbs, 2.68 mL for 45-88 lbs, and 4.02 mL for 89-132 lbs.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test material: Dog Spot-On ECS-28-99-1

Description:	Low viscosity clear liquid with a dull solvent odor
Lot No:	ECS-28-99-1
Purity:	Fipronil: 10.0% (102.0% of label claim) and Novaluron: 20.6% (103.0% of label claim)
Compound Stability:	Expiration date: January 13, 2014; ambient storage conditions
CAS Nos:	120068-37-3 (Fipronil) and 116714 (Novaluron)

2. Placebo control: Dog Spot-On Blank ECS-28-99-2

Description:	Liquid; according to information provided to this reviewer on April 9, 2013 from the registrant's representative this was the formulated product less the active ingredients.
Lot Nos:	ECS-28-99-2
Purity:	Not provided
Compound Stability:	Expiration date: January 13, 2014; ambient storage conditions
CAS #:	Not provided

3. Vehicle and/or positive control: Although not stated in the report, it was confirmed on April 9, 2013 by the registrant's representative that ECS-28-99-2 is the formulated product minus the active ingredients; this is consistent with the dosage given as the nominal percentage of other ingredients is 70.2%, and 0.702 x 0.67 mL (for dogs ≤ 10 kg) = 0.47 mL and 0.702 x 1.34 mL (for dogs > 10 kg) = 0.94 mL.

4. Test animals:

Species:	Dog	
Breed:	Beagle	
Age/weight at study initiation:	Puppies: 55-57 days old at treatment (day 0); males: 2.589-3.376 kg (5.71-7.443 lbs); females: 2.262-2.886 kg (4.987-6.362 lbs) Adult dogs: 11.3-13.8 months old at treatment (day 0): males: 8.61-12.66 kg (18.98-27.91 lbs); females: 7.91-9.59 kg (17.44-21.14 lbs)	
Source:	Ridglan Farms, Mount Horeb, WI	
Housing:	Puppies (from day -7 to the end of study): individually in stainless steel pens (~3 ft x 5 ft) Adult dogs: individually in chain-link fence and frame pens (~3.4 ft x 5.5 ft)	
Diet:	Puppies: commercial dry food (Purina® Puppy Chow); 300 gmms/puppy/day from day -7. Adult dogs: commercial dry food (Purina® Dog Chow); 250 grams/dog/day from day -14.	
Water:	Water from an on-site deep well, available *ad libitum*. Available in a water bowl for puppies and a stainless steel Lixit for adult dogs.	
Environmental conditions:	Temperature:	Puppies: 69.3-79.3° F; Adult dogs: 62.3-80.0° F.
	Humidity:	Puppies: 18-85%; Adult dogs: 15-102.9%
	Air changes:	"Appropriate hourly air exchanges."
	Photoperiod:	12 hours light/12 hours dark
Acclimation period:	14 days	

B. STUDY DESIGN:

1. **In life dates:** Start of acclimation (Day -14): January 23, 2012; Start (Day 0): February 7, 2012; End (Day 14): February 21, 2012.

2. **Animal assignment:** The study design is given in Table 1. From p. 12 of MRID 48843210: "On Day -1, puppies and adult dogs meeting the inclusion criteria...were randomized to treatment groups, based on the most recent body weight determinations (day -1), using Microsoft Excel® (Version 2003) random function. Within each age group and gender, the puppies/dogs were ranked by body weight in ascension and assigned to blocks, three (3) puppies/dogs per block. Thus, the three (3) lightest puppies/dogs were in "Block 1," the next three (3) puppies/dogs were in "Block 2," etc., until all puppies/dogs were assigned to a block. Within each block, each puppy/dog was assigned a random number generated using the RAND function. The first three puppies/dogs (within "Block 1") were assigned to Groups 1 through 3 with the lowest random number puppy/dog assigned to Group 1, the next highest random number assigned to Group 2, etc. This procedure was repeated for all remaining puppies/dogs within each successive block until each puppy/dog was assigned to a treatment group. Then, a single factor ANOVA (in Excel) was conducted with an alpha across treatment groups for body weight."

TABLE 1: Study design [a]

Test Group	Test Material	1X Dosing volume	Number of Doses	Cumulative Dosing Volume	Numbers of Animals Assigned			
					Puppies		Adult Dogs	
					Males	Females	Males	Females
A (3X)	Fipronil-Novaluron Spot-on	Puppies: 0.67 mL Adult dogs: 0.67 or 1.34 mL [b]	3 (at 1-hour intervals)	Puppies: 2.01 mL Adult dogs: 2.01 or 4.02 mL [c]	3	3	3	3
B (5X)	Fipronil-Novaluron Spot-on	Puppies: 0.67 mL Adult dogs: 0.67 mL or 1.34 mL [b]	5 (at 1-hour intervals)	Puppies: 3.35 mL Adult dogs: 3.35 or 6.70 mL [d]	3	3	3	3
C (5X)	Placebo Control	Puppies: 0.47 mL Adult dogs: 0.47 mL or 0.94 mL [e]	5 (at 1-hour intervals)	Puppies: 2.35 mL Adult dogs: 2.35 mL or 4.70 mL [f]	3	3	3	3

[a] Data taken from p. 17, MRID 48843210.
[b] 0.67 mL for puppies and adult dogs ≤ 10 kg (all puppies weighed ≤ 10 kg); 1.34 mL for adult dogs > 10 kg
[c] 2.01 mL for puppies and adult dogs ≤ 10 kg (all puppies weighed ≤ 10 kg); 4.02 mL for adult dogs > 10 kg
[d] 3.35 mL for puppies and adult dogs ≤ 10 kg (all puppies weighed ≤ 10 kg); 6.70 mL for adult dogs > 10 kg
[e] 0.47 mL for puppies and adult dogs ≤ 10 kg (all puppies weighed ≤ 10 kg); 0.94 mL for adult dogs > 10 kg
[f] 2.35 mL for puppies and adult dogs ≤ 10 kg (all puppies weighed ≤ 10 kg); 4.70 mL for adult dogs > 10 kg

3. **Dose selection rationale:** From p. 18 of MRID 48843210: "Dose selections were provided by the Sponsor based on previous testing." The dosages are consistent with those given on

the proposed label (dogs & puppies [8 weeks or older] up to 22 lbs: 0.67 mL; dogs 23-44 lbs: 1.34 mL; dogs 45-88 lbs: 2.68 mL; dogs 89-132 lbs: 4.02 mL).

4. Treatment: From information on p. 59 of MRID 48843210 the placebo control or test material, as appropriate, was applied topically on day 0 from either a calibrated syringe or pipette. The application was "...directly to the skin on the dorsal midline from the base of the skull to the interscapular region." The application directions on the proposed label state: "Squeeze tube firmly to apply all of the solution to the dog's skin [as a spot [on][to] the dog's back between the shoulder blades.][or][from the back of the neck to a point midway between the neck and tail.]" The directions to apply from the back of the neck to a point midway between the neck and tail [as a "stripe-on?] do not appear to be consistent with how the test material was applied in this study, particularly as there is the possibility that the dog could lick the region of its back midway between the neck and tail.

5. Statistics: From p. 123-124 of MRID 48843210:

Treatment was administered individually to each animal. The experimental unit was defined as the individual animal.

Data continuous in nature and collected over time were analyzed by RMANCOVA appropriate for a repeated measures experiment using the MIXED procedure of SAS. A compound symmetric structure was assumed for the covariance matrix given only 2 timepoints post-treatment were to be evaluated. Daily food consumption was condensed to weekly food consumption. Pre-treatment values were included as the covariate. The model included the main effects of "treatment group", "age group", "gender" and "time"; the two-way interactions "treatment group * age group", "treatment group * gender", "treatment group by time", "age group * gender", "age group * time" and "gender * time"; the three-way interactions " treatment group * age group * gender", " treatment group * age group * time", " treatment group * gender * time" and " age group * gender * time"; and the four-way interaction "treatment group * age group * gender * time". If the four-way interaction was statistically significant ($P < 0.05$), no further hypothesis testing was conducted given the small sample size. If the four-way interaction was not significant, and any of three-way interactions "treatment group * age group * gender", "treatment group * age group * time" or "treatment group * gender * time" were statistically significant ($P < 0.05$), no further hypothesis testing was conducted given the small sample size. Two-way interactions not involved in significant three-way interactions were assessed at $P < 0.05$. If two-way interactions involving treatment group were significant, the treatment group effects within age group and/or gender and/or time were assessed. Linear contrasts comparing the placebo to the 3X and placebo to the 5X groups were evaluated using an unadjusted alpha = 0.05. If none of the interactions were significant ($P > 0.05$), the main effect of treatment group was evaluated. If the main effect of treatment group was significant ($P < 0.05$), linear contrasts comparing the placebo to the 3X and placebo to the 5X groups were evaluated using an unadjusted alpha = 0.05. If the P-value for any interaction was greater than 0.25, the interaction was dropped from the model.

Treatment was administered individually to each animal. The experimental unit was defined as the individual animal.

Data continuous in nature and collected over time were analyzed by RMANCOVA appropriate for a repeated measures experiment using the MIXED procedure of SAS. A compound symmetric structure was assumed for the covariance matrix given only 2 timepoints post-treatment were to be evaluated. Daily food consumption was condensed to weekly food consumption. Pre-treatment values were included as the covariate. The model included the main effects of "treatment group", "age group", "gender" and "time"; the two-way interactions "treatment group * age group", "treatment group * gender", "treatment group by time", "age group * gender", "age group * time" and "gender * time"; the three-way interactions " treatment group * age group * gender", " treatment group * age group * time", " treatment group * gender * time" and " age group * gender * time"; and the four-way interaction "treatment group * age group * gender * time". If the four-way interaction was statistically significant ($P < 0.05$), no further hypothesis testing was conducted given the small sample size. If the four-way interaction was not significant, and any of three-way interactions "treatment group * age group * gender", "treatment group * age group * time" or "treatment group * gender * time" were statistically significant ($P < 0.05$), no further hypothesis testing was conducted given the small sample size. Two-way interactions not involved in significant three-way interactions were assessed at $P < 0.05$. If two-way interactions involving treatment group were significant, the treatment group effects within age group and/or gender and/or time were assessed. Linear contrasts comparing the placebo to the 3X and placebo to the 5X groups were evaluated using an unadjusted alpha = 0.05. If none of the interactions were significant ($P > 0.05$), the main effect of treatment group was evaluated. If the main effect of treatment group was significant ($P < 0.05$), linear contrasts comparing the placebo to the 3X and placebo to the 5X groups were evaluated using an unadjusted alpha = 0.05. If the P-value for any interaction was greater than 0.25, the interaction was dropped from the model.

C. METHODS:

1. Observations:

a. **General health observations:** The animals were observed at least twice daily (typically AM and PM).

b. **Clinical observations:** These were initiated on day 0 at pre-dose and at 1, 2, 3 and 4 hours post-treatment of the final subapplication. After day 0, observations were made twice daily through the study termination.

Personnel responsible for clinical observations were blinded to treatment assignments.

c. **Physical examinations:** All animals received physical examinations from a veterinarian on days -7, 7 and 14.

2. **Body weights:** Body weights were determined on days -14, -1, 7 and 14.

3. **Food consumption:** Individual food consumption values were measured and recorded daily. For puppies, this was from day -7 through day 13; for the adult dogs this was from day -14 through day 13.

4. **Clinical pathology:** On days -7, 1, and 7, blood was collected for hematology, clinical chemistry, and coagulation measurements. Puppies were not fasted before blood was taken; adult dogs were fasted for an unspecified period of time before blood was collected. The CHECKED parameters were measured:

a. **Hematology and coagulation:**

X	Hematocrit (HCT)*	X	Leukocyte differential count* (absolute and percentage)
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count		Reticulocyte count (percent and absolute)
	Blood clotting measurements		Morphology (RBC)
X	(Activated Partial Thromboplastin time)*		Heinz body formation (percent and absolute)
	(Clotting time)		Red cell distribution width (RDW)
X	(Prothrombin time)*		Hemoglobin distribution width (HDW)
			Fibrinogen

* Recommended for companion animals safety evaluation based on OCSPP 870.7200

b. **Clinical chemistry:**

	ELECTROLYTES		OTHER
X	Calcium*	X	Albumin*
X	Chloride*	X	Creatinine*
	Magnesium	X	Urea nitrogen (BUN)*
X	Phosphorus*		Cholesterol
X	Potassium*	X	Globulins*
X	Sodium*	X	Glucose*
	ENZYMES	X	Total bilirubin*
X	Alkaline phosphatase (ALK)*	X	Direct bilirubin*
	Cholinesterase (ChE)		Indirect bilirubin
	Creatine phosphokinase	X	Total protein (TP)*
	Lactic acid dehydrogenase (LDH)		Triglycerides
X	Alanine aminotransferase (ALT/also SGPT)*		Serum protein electrophoresis
X	Aspartate aminotransferase (AST/also SGOT)*	X	Albumin/globulin ratio
	Sorbitol dehydrogenase (SDH)		
X	Gamma glutamyl transferase (GGT)		
	Glutamate dehydrogenase		

* Recommended for a companion animal safety evaluation based on OCSPP 870.7200.

5. **Urinalysis:** Urinalysis is not required for companion animal safety studies and was not done as part of the current study.

6. **Sacrifice and pathology:** There were no deaths or moribund sacrifices during the study. Terminal sacrifices and gross necropsies were not done and are not required under OCSPP 870.7200.

II. RESULTS

A. **ACTUAL DOSES ADMINISTERED:** The mg/kg doses of the active ingredients are given in Tables 2a and 2b, below:

Test Group	Test Material	Cumulative Dose of Formulation (g) (1 mL=1.0588 g)	Cumulative Dose of Fipronil (mg)/puppy	Cumulative Dose of Novaluron (mg)/puppy	Puppy weight range (kg)	Mean Puppy weight (kg)	Dose range of Fipronil *(Novaluron)* mg/kg	Mean Dose of Fipronil *(Novaluron)* mg/kg
A (3X)	Fipronil-Novaluron Spot-on	2.128 g/puppy	208.5	425.6	2.262-3.254	2.755	64.1-92.2 *(130.8-188.2)*	75.7 *(154.5)*
B (5X)	Fipronil-Novaluron Spot-on	3.547 g/puppy	347.6	709.4	2.424-3.254	2.841	106.8-143.4 *(218.0-292.7)*	122.4 *(249.7)*
C (5X)	Placebo Control	2.488 g/puppy	0	0	2.262-3.376	2.790	0 *(0)*	0 *(0)*

TABLE 2b: mg/kg doses of the active ingredients (adult dogs)

Test Group	Test Material	Cumulative Dose of Formulation (g) (1 mL=1.0588 g)	Cumulative Dose of Fipronil (mg)/dog	Cumulative Dose of Novaluron (mg)/dog	Dog weight range (kg)	Mean Dog weight (kg)	Dose range of Fipronil *(Novaluron)* mg/kg	Mean Dose of Fipronil *(Novaluron)* mg/kg
A (3X)	Fipronil-Novaluron Spot-on	2.128 g/dog (≤ 10 kg) 4.256/dog (> 10 kg)	208.5 (≤ 10 kg) 417.1 (> 10 kg)	425.6 (≤ 10 kg) 851.3 (> 10 kg)	8.24-12.66	10.32	22.7-37.2 *(46.4-76.0)*	29.5 *(60.2)*
B (5X)	Fipronil-Novaluron Spot-on	3.547 g/dog (≤ 10 kg) 7.094 g/dog (>10 kg)	347.6 (≤ 10 kg) 695.2 (>10 kg)	709.4 (≤ 10 kg) 1418.8 (> 10 kg)	8.43-12.49	10.01	35.3-60.7 *(72.1-123.8)*	45.2 *(92.1)*
C (5X)	Placebo Control	2.488 g/dog (≤ 10 kg) 4/976 g/dng (>10 kg)	0	0	7.91-11.66	9.22	0 *(0)*	0 *(0)*

B. OBSERVATIONS:

1. **Clinical signs:** The observed clinical signs for puppies are given in Table 3 and for adults in Table 4.

Table 3 Individual Animal Abnormal Clinical Observations

Gender	Dose	Study ID	Clinical Observation	Description	Study Day(s)
Puppies:					
M	3x Treatment	AM1:VLZ-1	feces	loose	1
			feces	diarrhea	3
			vomiting	no description	3
M		AM2:WLZ-1	feces	loose	8,10
			feces	diarrhea	9
M		AM3:VCZ-1	eyes	discharge	3
			feces	loose	Pre Dose
			seizure	moderate	11
F		AF1:UVY-1	feces	loose	4,5
			eyes	discharge,OD	9
F		AF2:UUY-1	feces	loose	4hr Post
			vomiting	no description	3
F		AF3:WQY-1	feces	dry	Pre Dose
			eyes	discharge,OU	9
M	5x Treatment	BM1:WPZ-1	no abnormal findings		
M		BM2:WOZ-1	no abnormal findings		
M		BM3:VYZ-1	no abnormal findings		
F		BF1:VRY-1	feces	loose	2,3,4,5,8
			feces	diarrhea	3
F		BF2:UWY-1	vomiting	no description	Pre Dose
			eyes	discharge, OU	5
F		BF3:VZY-1	no abnormal findings		
M	5x Control	CM1:VOZ-1	feces	loose	3hr Post,9
			respiration	rapid	Pre Dose
			behavioral attitude	circling	Pre Dose
			skin condition	flakes of skin around shoulder	7,8,9,10
M		CM2:USZ-1	no abnormal findings		
M		CM3:VDZ-1	vomiting	food	1
			skin condition	flakes of skin around shoulder	9
F		CF1:WSY-1	feces	dry	Pre Dose
			feces	loose	5
			feces	diarrhea	3,5
			eyes	discharge, OD	4
			eyes	discharge, OU	8
F		CF2:V8Y-1	feces	loose	Pre Dose,4,5,7,8,10,11,12,13
			feces	diarrhea	2hr Post,1,2,3,6,8
F		CF3:UTY-1	eyes	discharge, OU	8

Table 3 Key: OD = Right; OS = Left; OU = Both

Table 4. Individual animal (adult dog) Abnormal Clinical Observations.

Gender	Dose	Study ID	Clinical Observation	Description	Study Day(s)
Adults:					
M	3x Treatment	AM4:QJD-1	feces	loose	3,4,5,6,7,8,14
			feces	diarrhea	2
M		AM5:IED-1	feces	loose	3,5,9,13
			feces	diarrhea	4
			skin condition	irritation, both ears	4,5,6,7,8,9,10,12,13,14
M		AM6:UGD-1	feces	loose	2hr Post,2,3,4,5,6,7,8,9,13
			skin condition	rough	3
			skin condition	irritation, both ears	4,6,7,8,9,10,11,12,13,14
F		AF4:SFA-1	feces	loose	2
			feces	diarrhea	4
			eyes	discharge, OU	7
			eyes	discharge, OS	8
			skin condition	irritation, both ears	4,5,6,7,8,9
F		AF5:KZC-1	feces	loose	8,9,10,11,12,13,14
			feces	diarrhea	2,3,4,5,6,9
			eyes	discharge, OS	4,7
			skin condition	irritation, both ears	4,5,6,7,8,9,10,12,13,14
F		AF6:QSA-1	feces	loose	1hr Post,2 hr Post, 3hr Post,3,5,8,9,10,11,13,14
			feces	diarrhea	2,7
			eyes	discharge, OD	4,7,14
			skin condition	irritation, both ears	4,6,7
M	5x Treatment	BM4:OXD-1	feces	loose	1hr Post,2 hr Post, 3hr Post,1,3,5,6,7,8,9,10,11, 12,13,14
			feces	diarrhea	3,4
M		BM5:QXD-1	feces	dry	4
			feces	loose	1hr Post,2 hr Post, 3hr Post,1,3,5,6,7,13
			feces	diarrhea	8
			skin condition	scratch between shoulder and right ear	Pre Dose
			skin condition	irritation, both ears	5,6,7,8,9
M		BM6:LYD-1	feces	loose	1,2,3,6,7,8,9
			feces	diarrhea	7,9
			skin condition	irritation, both ears	4,5,6,7,8,9,10,12,13,14
F		BF4:KCC-1	feces	loose	12,14
			skin condition	irritation, right ear	5,6,7,8
F		BF5:GAY-0	feces	loose	3
			eyes	discharge, OS	14
			skin condition	irritation, left ear	5,6,7,12,13,14
F		BF6:HAC-1	feces	loose	2,3
			eyes	discharge, OS	5,6,7,10,13,14
			skin condition	irritation, both ears	5

Table 4 (continued) Individual animal (adult dog) Abnormal Clinical Observations

Gender	Dose	Study ID	Clinical Observation	Description	Study Day(s)
Adults					
M	5x Control	CM4:SPD-1	feces	Loose	1hr Post, 2 hr Post, 1,3,4,5,6,7,9,10,12,13,14
			feces	Diarrhea	2,8
			feces	bloody diarrhea	11
			skin condition	Rough	3
			skin condition	irritation, right ear	5
			skin condition	irritation, both ears	14
			eyes	discharge, OS	4,5,6,7,8,9,10,11,13,14
M		CM5:FXZ-0	feces	Loose	3,4,6,10,11,12,13,14
			feces	Diarrhea	2
			skin condition	scratch between shoulder and left ear	Pre Dose
M		CM6:QED-1	feces	Dry	4
			feces	Loose	2hr Post,1,3,5,6,7,8,10,11, 12,14
			feces	Diarrhea	2,13
			skin condition	Rough	3
			skin condition	irritation, both ears	4,5,6,7,8,9
F		CF4:XPA-1	feces	Loose	9
			locomotion/ musculature	non weight bearing, right hind	Pre Dose, 3hr Post, 1
			eyes	discharge, OS	6,13
			eyes	discharge, OD	10
			eyes	discharge, OU	10
			skin condition	irritation, both ears	4,5,6,7,8,9,10,13,14
F		CF5:REA-1	feces	Loose	6,7,8,10
			skin condition	irritation, both ears	4
			eyes	discharge, OD	5
			vomiting	no description	7
F		CF6:QCA-1	feces	Loose	2,3,8
			skin condition	irritation, both ears	4,12
			skin condition	irritation, right ear	13,14
			vomiting	no description	14

Post-application clinical observations included seizure activity in a Group A (3X) male puppy [AM3: VCZ-1] on day 11, described [p. 22 of MRID 48843210] as a "self-limited episode…that did not require medical intervention." Also from p. 22: "As this self-limited event occurred only once 11 days after treatment in a 3X puppy, and no other animals, including all the 5X animals did not experience this, it was judged to not be treatment-related." The only other mention of this event is in Table 3 on p. 72 of MRID 48843210, where the seizure [described as "moderate"] is reported for day 11. Other observations included gastrointestinal findings (primarily loose feces and diarrhea [including one incident of bloody diarrhea in a 5X control animal on day 11] with occasional incidents of vomiting), discharge from one or both eyes, and irritation in one or both ears (occurring only in adults of all groups, appearing 4-5 days after treatment, often persisting through day 14).

2. **Quantitative physical signs parameters:** There were no indications of any treatment-related effects on heart rate or respiratory rate as measured on days 7 and 14.

3. **Local effects at the application site:** Two control puppies had flaking of the skin (one on days 7 through 10, the other on day 9) at the application site without underlying redness or other irritation. One 3X adult had "rough" skin (presumably at the application site) on day 3, as did two 5X controls.

4. **Mortality:** There were no deaths or moribund sacrifices.

C. **BODY WEIGHT AND WEIGHT GAIN:** Body weight data are given in Tables 5A (puppies) and5B (adult dogs). There were no treatment-related effects on body weight or body weight gain. All of the puppies gained weight over the course of the study.

Table 5A. Body Weight Changes in Puppies

Individual Animal No.	Weight change (kg) Day -14 to Day -1	Weight change (kg) Day -1 to Day 7	Weight change (kg) Day 7 to Day 14
AM1:VLZ-1	0.469	0.261	0.507
AM2:WLZ-1	0.668	0.507	0.589
AM3:VCZ-1	0.229	1.279	0.652
AF1:UVY-1	0.916	0.682	0.614
AF2:UUY-1	0.545	0.608	0.323
AF3:WQY-1	0.352	0.593	0.722
Group A Means ± S.D.	0.530 ± 0.243	0.655 ± 0.339	0.568 ± 0.139
BM1:WPZ-1	0.736	0.308	0.724
BM2:WOZ-1	0.957	0.644	0.885
BM3:VYZ-1	0.120	1.074	0.428
BF1:VRY-1	0.344	0.310	0.532
BF2:UWY-1	0.719	0.649	0.507
BF3:VZY-1	0.408	0.519	0.353
Group B Means ± S.D.	0.547 ± 0.309	0.584 ± 0.284	0.572 ± 0.198
CM1:VOZ-1	0.457	0.473	0.630
CM2:USZ-1	1.058	0.630	0.624
CM3:VDZ-1	0.695	0.587	0.679
CF1:WSY-1	0.478	0.476	0.502
CF2:VSY-1	0.336	0.328	0.372
CF3:UTY-1	0.559	0.725	0.442
Group C Means ± S.D.	0.597 ± 0.255	0.537 ±0.140	0.542 ± 0.121

Table 5B. Body Weight Changes in Adult Dogs			
Individual Animal No.	Weight change (kg) Day -14 to Day -1	Weight change (kg) Day -1 to Day 7	Weight change (kg) Day 7 to Day 14
AM4:QJD-1	-0.08	-0.03	+0.16
AM5:IED-1	+0.38	-0.12	+0.13
AM6:UGD-1	-0.19	-0.38	-0.30
AF4:SFA-1	-0.06	+0.06	+0.17
AF5:KZC-1	+0.15	+0.00	+0.08
AF6:QSA-1	+0.29	-0.34	+0.26
Group A Means ± S.D.	+0.08 ± 0.23	-0.14 ± 0.18	+0.08 ± 0.20
BM4:OXD-1	+0.22	+0.03	+0.10
BM5:QXD-1	-0.06	-0.25	+0.00
BM6:LYD-1	+0.31	-0.21	+0.18
BF4:KCC-1	-0.02	-0.49	+0.18
BF5:GAY-0	-0.07	-0.25	+0.24
BF6:HAC-1	-0.15	-0.21	+0.20
Group B Means ± S.D.	+0.04 ± 0.18	-0.23 ± 0.17	+0.15 ± 0.09
CM4:SPD-1	+0.18	-0.09	+0.05
CM5:FXC-0	+0.30	-0.33	+0.39
CM6:QED-1	-0.03	-0.04	+0.14
CF4:XPA-1	+0.26	-0.33	+0.43
CF5:REA-1	+0.24	-0.58	+0.31
CF6:QCA-1	-0.02	-0.52	+0.43
Group C Means ± S.D.	+0.16 ± 0.14	-0.32 ±0.22	+0.29 ± 0.16

Although some adult dogs did have small weight losses between some of the measuring intervals, these were of biologically insignificant magnitude and showed no indications of a treatment-related pattern.

D. FOOD CONSUMPTION: Mean group food consumption values for puppies were slightly lower on Day -1, possibly associated with the stress of being weighed. There was no indication of an effect on day 0 (day of application) or on subsequent days.

Table 6A. Food Consumption/Day (g) - Puppies

Individual Animal No.	Day -3	Day -2	Day -1	Day 0	Day 1	Day 2	Day 3	Day 7	Day 13
AM1:VLZ-1	102	209	144	141	158	113	158	163	200
AM2:WLZ-1	123	184	102	117	160	162	121	139	197
AM3:VCZ-1	94	203	157	171	248	161	137	194	154
AF1:UVY-1	113	224	111	175	200	198	145	149	270
AF2:UUY-1	85	184	80	81	103	132	160	116	179
AF3:WQY-1	55	172	96	151	129	168	151	204	121
Group A Means ± S.D.	95.3 ±23.9	196.0 ±19.3	115.0 ±29.6	139.3 ±35.5	166.3 ±51.6	155.7 ±29.6	145.3 ±14.6	160.8 ±33.5	186.8 ±50.3
BM1:WPZ-1	100	191	76	141	153	154	156	169	200
BM2:WOZ-1	164	193	177	176	255	142	137	260	155
BM3:VYZ-1	80	168	75	175	142	n.d.	273	201	252
BF1:VRY-1	96	126	74	84	32	49	72	124	149
BF2:UWY-1	97	168	122	186	160	167	155	153	151
BF3:VZY-1	69	122	5	87	163	124	121	138	154
Group B Means ± S.D.	101.0 ±33.1	161.3 ±30.9	88.2 ±57.4	141.5 ±46.0	150.8 ±71.1	127.2 ±46.5	152.3 ±66.7	174.2 ±49.8	176.8 ±41.5
CM1:VOZ-1	76	177	65	170	137	138	132	164	150
CM2:USZ-1	143	224	109	200	135	159	204	182	246
CM3:VDZ-1	89	142	182	195	167	161	192	193	233
CF1:WSY-1	81	152	81	123	132	119	104	158	141
CF2:VSY-1	55	168	89	152	124	98	136	162	120
CF3:UTY-1	69	178	92	143	131	161	139	167	180
Group C Means ± S.D.	85.5 ±30.4	173.5 ±28.5	103.0 ±41.3	163.8 ±30.2	137.7 ±15.0	139.3 ±26.3	151.2 ±38.5	171.0 ±13.6	178.3 ±51.3

For the adult dogs, group mean food consumption values were noticeably lower on day 0 (the day of application), and this was more pronounced in females but was consistent across all 3 groups. This may have been associated with the stress (excitement?) from the interaction with personnel during dosing, but in any case food consumption values returned to normal on day 1 so that even if this was considered to be an adverse effect it was reasonably transient.

Table 6B. Food Consumption/Day (g) – Adult dogs									
Individual Animal No.	Day -3	Day -2	Day -1	Day 0	Day 1	Day 2	Day 3	Day 7	Day 13
AM4:QJD-1	250	250	250	250	250	250	250	250	250
AM5:IED-1	250	250	250	250	250	250	250	250	250
AM6:UGD-1	250	250	250	250	250	250	250	250	250
AF4:SFA-1	194	250	227	89	238	250	250	250	250
AF5:KZC-1	204	250	250	85	250	250	250	250	250
AF6:QSA-1	250	250	169	2	255	250	250	275	250
Group A Means ± S.D.	233 ±26.5	250.0 ±0.0	232.7 ±32.5	154.3 ±109.3	248.8 ±5.7	250.0 ±0.0	250.0 ±0.0	254.2 ±10.2	250.0 ±0.0
BM4:OXD-1	250	250	250	250	250	250	250	250	250
BM5:QXD-1	250	250	250	250	250	250	250	250	250
BM6:LYD-1	250	250	250	2	275	250	250	250	250
BF4:KCC-1	250	207	129	122	125	226	232	250	250
BF5:GAY-0	181	137	137	4	157	216	133	236	221
BF6:HAC-1	166	223	114	44	250	250	250	250	250
Group B Means ± S.D.	224.5 ±39.8	219.5 ±44.2	188.3 ±68.0	112.0 ±115.4	217.8 ±61.1	240.3 ±15.3	227.5 ±46.9	247.7 ±5.7	245.2 ±11.8
CM4:SPD-1	250	250	250	250	250	250	250	250	250
CM5:FXZ-0	209	205	205	100	238	250	250	275	212
CM6:QED-1	224	250	250	2	275	250	250	250	184
CF4:XPA-1	246	250	129	119	183	250	250	250	250
CF5:REA-1	250	250	250	145	250	182	157	275	250
CF6:QCA-1	250	193	158	80	94	179	148	250	250
Group C Means ± S.D.	238.2 ±17.5	233.0 ±26.6	207.0 ±53.0	116.0 ±81.7	215.0 ±66.7	226.8 ±35.9	217.5 ±50.4	258.3 ±12.9	232.7 ±28.3

E. BLOOD ANALYSES:

1. **Hematology and coagulation parameters:** No treatment-related or biologically relevant changes in hematology or coagulation parameters were observed.

2. **Clinical chemistry:** No treatment-related or biologically relevant changes in clinical chemistry parameters were observed.

III. DISCUSSION and CONCLUSIONS

A. **INVESTIGATORS' CONCLUSIONS:** The study author concluded that no treatment-related clinical signs or effects were observed in puppies 8 weeks of age or in adult dogs treated once topically with three (3) or five (5) applications of the test substance, Fipronil-Novaluron Spot-on compared with similar animals receiving five (5) applications of a placebo control substance.

B. EPA REVIEWER COMMENTS:

It is concluded that the margin of safety in adult and 8-week-old beagles administered Dog Spot-On ECS-28-99-1 (Fipronil: 10.0%; Novaluron: 20.6%) is at least 5X the recommended dosing volumes of 0.67 mL for dogs and puppies ≤ 10 kg and 1.34 mL for dogs >10 kg and ≤ 20 kg. The study also supports dosages of 2.68 mL for dogs >20 kg and ≤ 40 kg, and 4.02 mL for dogs >40 kg and ≤ 60 kg. Since the mean weight of the 5X (Group B) puppies was 2.84 ± 0.28 kg (=6.26 ± 0.62 lbs) the data will support use on dogs and puppies (8 weeks and older) with a minimum weight of 7 lbs which must be declared on the label.

1. **DP BARCODE:** 404003
2. **PC CODES:** 124002 (Novaluron: 20%); 129121 (Fipronil: 9.8%)
3. **CURRENT DATE:** April 16, 2013
4. **TEST MATERIAL:** Dog Spot-On ECS-28-99-1, a low viscosity clear liquid with a dull solvent odor, containing Fipronil 10.0% (102.0% of label claim) and Novaluron: 20.6% (103.0% of label claim)

Study/Species/Lab Study # / Date	MRID	Results	Tox. Cat.	Core Grade
Companion animal safety/8-week-old beagle puppies and 11.3 to 13.8 month adult dogs/Sinclair Research Center, Inc., Auxvasse, MO/Project No. S11227/OCR/June 5, 2012	48843210	Groups consisting of three 8-week-old (±1 day) and three adult (>11 months old) beagles/sex were treated on day 0 with either 3 1X applications of formulation (Group A); 5 1X applications of formula- tion (Group B) or 5 1X applications of formulated product minus the active ingredients. Applications were spaced 1 hour apart. Test material or placebo was applied directly to skin on the dorsal mid-line to interscapular region. Dogs were observed for 14 days. Post application clinical observations included seizure activity in a Group QA (3X) male puppy on day 11 that did not require medical intervention. There were no treatment or dose-related effects on mortality, body weight, food consumption, hematology, coagulation, or clinical chemistry parameters. **The margin of safety in adult and 8-week-old beagles administered Dog Spot-On ECS-28-99-1 is at least 5X the recommended dosing volumes of 0.67 mL for dogs and puppies ≤ 10 kg and 1.34 > 10 kg and ≤ 20 kg. The study also supports dosages of 2.68 mL for dogs >20 kg and ≤ 40 kg, and 4.02 mL for dogs >40 kg and ≤ 60 kg. Since the mean weight of the 5X (Group B) puppies was 2.84 ± 0.28 kg (=6.26±0.62 lbs) the data will support use on dogs and puppies (8 weeks and older) with a minimum weight of 7 lbs which must be declared on the label.**	n/a	Acceptable

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: 21-MAY-2013

SUBJECT: **Novaluron:** Human-Health Risk Assessment for Proposed Section 3 Uses as a Dog Spot-On and in Cattle and Poultry Operations and Horse Barns.

PC Code: 124002	**DP Barcodes:** D404422; D406091
Decision Nos.: 465891; 461013	**Registration Nos.:** 53883-NEW; 53883-xxx
Petition No.: NA	**Regulatory Action:** Section 3
Risk Assessment Type: Single Chemical Aggregate	**Case No.:** 7615
TXR No.: NA	**CAS No.:** 116714-46-6
MRID No.: NA	**40 CFR:** §180.598

FROM: Julie L. Van Alstine, MPH, Environmental Health Scientist
Anwar Y. Dunbar, Ph.D., Pharmacologist
Lata Venkateshwara, Environmental Scientist
Risk Assessment Branch 1 (RAB1)
Health Effects Division (HED; 7509P)

THROUGH: Dana M. Vogel, Acting Branch Chief
George F. Kramer, Ph.D., Branch Senior Chemist
RAB1/HED (7509P)

TO: John Hebert (RM 07)/Autumn Metzger/Jennifer Gaines
Registration Division (RD; 7505P)

The HED of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential, and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from all registered and proposed uses of novaluron (*N*-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy] phenyl]amino]carbonyl]-2,6-difluorobenzamide). A summary of the findings and an assessment of human risk resulting from the registered and proposed uses for novaluron are provided in this document. The risk assessment was provided by Julie Van Alstine (RAB1), the hazard characterization by Anwar Dunbar (RAB1), and the occupational and residential exposure assessments were provided by Lata Venkateshwara (RAB1).

The most recent human-health risk assessment was conducted in conjunction with a request for the use of novaluron on peanut and soybean (Memo, J. Van Alstine, *et al.*, 15-MAY-2013; D400705).

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1.0 Executive Summary

Background: Novaluron, a benzoylphenyl urea compound, is a pesticide chemical belonging to the class of insecticides called insect-growth regulators (IGRs). Tolerances for residues of novaluron are established under 40 CFR §180.598 in/on a wide variety of crops at levels ranging from 0.05 to 50 ppm. Tolerances for residues of novaluron are also established in/on the following livestock commodities: eggs, milk, milk fat, and the meat, fat, kidney, liver, and meat byproducts (except kidney and liver) of cattle, goat, horse, sheep, poultry, and hog. Additionally, novaluron is registered for use in food and feed handling establishments, and a tolerance of 0.01 ppm has been established for residues in/on food and feed commodities other than those covered by a higher tolerance as a result of use on growing crops.

Control Solutions, Inc. (CSI) has submitted a Section 3 request to register the product CSI Fipronil + Novaluron for use as a monthly topical solution for continuous protection against fleas, ticks, flea eggs, flea larvae (mosquitoes), and chewing lice on dogs. CSI's Fipronil + Novaluron product contains the active ingredients fipronil (9.8%) and novaluron (20%). The proposed product can be used by homeowners and by commercial applicators. The proposed spot-on product label allows for application to four dog-weight ranges: small, up to 22 pounds (lbs); medium, 23 to 43 lbs; intermediate, 45 to 88 lbs; and large, 89 to 132 lbs. The product is not proposed for use on cats. This risk assessment addresses novaluron only.

Additionally, CSI has submitted a Section 3 request to register the product Novaluron® 0.2G, which contains 0.2% novaluron, for use to control stable fly larvae in cattle operations and horse barns and to control litter beetles in poultry operations. Novaluron® 0.2G is a granule applied by dry scattering to fly breeding sites, including manure, in cattle and poultry operations and horse barns of horses not intended for slaughter or food. It acts as a growth regulator and affects the formation of fly and beetle larvae; it does not kill adult flies or beetles. The application rate for cattle operations and horse barns is two pounds per 200 square feet (0.8 lb ai/A; corresponds to 0.00002 lb ai/ft^2). The application rate for poultry operations is four pounds per 200 square feet (1.6 lb ai/A; corresponds to 0.00004 lb ai/ft^2). The application treatment interval depends on the management and housing systems as well as on climatic conditions. It can vary from 21 days up to several months.

There are no proposed or HED-recommended tolerances associated with the proposed dog spot-on and cattle and poultry operation and horse barn uses of novaluron.

Hazard Assessment: Novaluron has low acute toxicity via the oral (Toxicity Category IV), dermal (Toxicity Category III), and inhalation routes (Toxicity Category IV). No ocular (Toxicity Category IV) or dermal irritation (Toxicity Category IV) was noted. Novaluron is not a dermal sensitizer. In subchronic and chronic toxicity studies, novaluron primarily produced hematotoxic effects (toxicity to blood) such as methemoglobinemia, decreased hemoglobin, decreased hematocrit, and decreased red blood corpuscles (RBCs or erythrocytes) that were associated with compensatory erythropoiesis. No maternal and/or developmental toxicity was observed in animals tested up to the limit dose in either the rat or the rabbit developmental toxicity studies. In the two-generation reproductive toxicity study, increased spleen weights were observed in parents and offspring at the same dose, and reproductive toxicity was observed in males only at a higher dose. Neurotoxic effects, including clinical signs, changes in functional-observation battery (FOB) parameters, and neuropathology were observed following a single dose at the limit dose only (2000 mg/kg/day) in the acute neurotoxicity study in rats. However, no signs of neurotoxicity or neuropathology were observed following repeated dosing

in the subchronic neurotoxicity study in rats at similar doses, no evidence of neuropathology was observed in subchronic and chronic toxicity studies in rats, mice, or dogs, and novaluron is not considered acutely toxic (LD_{50} >5000 mg/kg). Therefore, RAB1 toxicologists reaffirmed the HED Hazard Identification Assessment Review Committee (HIARC) conclusion that there is not a concern for neurotoxicity resulting from exposure to novaluron. Potential signs of immunotoxicity occurred at twice the limit dose and consisted only of a decreased anti-sheep red blood cell (SRBC) response in female rats. There was no evidence of either carcinogenic or genotoxic potential and novaluron has been classified as "not likely to be carcinogenic to humans" based on the lack of evidence for carcinogenicity in mice and rats.

Consistent with previous risk assessments for novaluron (Memo, J. Van Alstine, *et al.*, 15-MAY-2013; D400705; Memo, L. Venkateshwara, *et al.*, 15-SEP-2011; D377471; Memo, J. Van Alstine, *et al.*, 23-FEB-2010; D364307), the novaluron risk assessment team recommends that the 10X Food Quality Protection Act Safety Factor (FQPA SF) be reduced to 1X for all exposure scenarios, as discussed in Section 4.4.

Exposure/Risk Assessment Characterization: The proposed uses do not impact the dietary exposure assessment; however, the details from a recent dietary exposure assessment have been included since food and drinking water exposures contribute to the aggregate assessment. An acute dietary assessment was not conducted for novaluron because an endpoint of concern attributable to a single dose was not identified. The most recent chronic dietary exposure and risk assessment was conducted based on registered uses and recently proposed uses on peanuts and soybeans. The chronic assessment directly incorporated drinking water estimates. Assumptions for the chronic dietary assessment included average field trial residues, tolerance-level residues for proposed commodities, anticipated residues (ARs) for meat, milk, hog, and poultry commodities, average percent crop treated (PCT) data for apples, cabbage, cauliflower, cotton, pears, potatoes, strawberries, and tomatoes, and percent crop treated for new use (PCTn) data for grain sorghum and sweet corn. For the remaining food commodities, 100% crop treated (CT) was assumed. The registered food handling use was also incorporated into the dietary assessment. Empirical processing factors for apple juice (translated to pear and stone fruit juice), cottonseed oil, dried plums, and tomato paste and purée, and DEEM (ver. 7.81) default processing factors for the remaining processed commodities were also used. All exposure and risk estimates were not of concern. A cancer dietary assessment was not conducted because novaluron is classified as "not likely to be carcinogenic to humans."

The proposed dog spot-on product is anticipated to result in short-, intermediate-, and long-term residential exposures. In addition, there are registered residential indoor uses for novaluron that were assessed previously. The proposed use in cattle and poultry operations and horse barns is not expected to result in residential exposures based on the proposed use pattern. The non-occupational (residential) use of the proposed dog spot-on product is anticipated to result in dermal exposures for adult handlers. In addition, residential post-application dermal exposures are expected for adults and children 1 to <2 years old, and incidental oral exposures for children 1 to <2 years old. A dermal endpoint was not selected for any exposure duration; therefore, quantitative dermal assessments were not conducted. In addition, based on the proposed spot-on use and the vapor pressure for novaluron, inhalation exposure is considered negligible for all exposure durations; therefore, only incidental oral exposures/risk estimates were assessed for the proposed product. All children incidental oral post-application risk estimates for all durations of exposure to treated pets resulted in margins of exposure (MOEs) greater than 100 and are not of concern to HED. In addition, all short-term residential handler and post-application scenarios

previously assessed for the registered indoor uses resulted in MOEs greater than 100 and are not of concern to HED.

For the proposed and registered uses, human-health aggregate risk assessments have been conducted for short- and intermediate-term aggregate exposure (food + drinking water + residential) scenarios. Even though there are long-term residential exposures from the proposed dog spot-on use, the intermediate-term aggregate assessment is protective of chronic aggregate exposure since there is no progression of effects in the database, and there is only one point of departure (POD) for all durations of incidental oral exposure. An acute aggregate assessment was not conducted for novaluron because an endpoint of concern attributable to a single dose was not identified. A cancer aggregate risk assessment was not performed because novaluron was classified as "not likely to be carcinogenic to humans." All potential exposure pathways were assessed in the aggregate risk assessment as a conservative, health-protective measure. No aggregate risk estimates exceed HED's level of concern (LOC) for the scenarios listed above.

There is the potential for occupational exposures of veterinarians, veterinary assistants, and groomers as a result of the proposed spot-on product to dogs; however, since dermal PODs were not selected for any exposure duration, dermal exposures were not quantitatively assessed. In addition, occupational inhalation exposure from application of the spot-on product is considered to be negligible and was not quantitatively assessed. A quantitative assessment of occupational post-application exposure from the proposed novaluron spot-on product was also not conducted since occupational post-application activities are expected to be significantly less than residential post-application exposures.

Based on the proposed use in cattle and poultry operations and horse barns, occupational handler exposure is expected to occur for short- and intermediate-term durations to novaluron during loading, applying, and other handling activities. Since dermal PODs were not selected for any exposure duration, dermal exposures were not quantitatively assessed. The occupational handler short- and intermediate-term non-cancer inhalation exposure risk estimates are not of concern to HED with baseline attire for all loader/applicator scenarios. No personal-protective equipment (PPE), except gloves, was recommended on the label. There are no site-specific post-application activities performed by workers after treating cattle operations, horse barns, and poultry operations with novaluron; therefore, a quantitative post-application exposure assessment was not performed.

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. Please refer to Appendix C for a discussion of the human study data used in this risk assessment.

2.0 HED Recommendations

Provided that CSI updates its registration request to indicate that the use in cattle and poultry operations is a food use, there are no chemistry, residential, occupational, or toxicology data deficiencies at this time for either registration request.

2.1 Tolerance Considerations

2.1.1 Recommended Tolerances

Tolerances are not required for the proposed dog spot-on use. Although the proposed use in cattle and poultry operations and horse barns may result in exposure to livestock, this exposure is anticipated to be insignificant when compared to the exposure resulting from the currently registered uses. Therefore, revised livestock tolerances are not required. Additionally, crops are not likely to have quantifiable residues due to the application of novaluron-treated manure to fields, so tolerances for indirect or inadvertent residues are not required as a result of the proposed use.

2.1.2 International Harmonization

Since there are no proposed or HED-recommended tolerances, harmonization is not an issue for these registration requests.

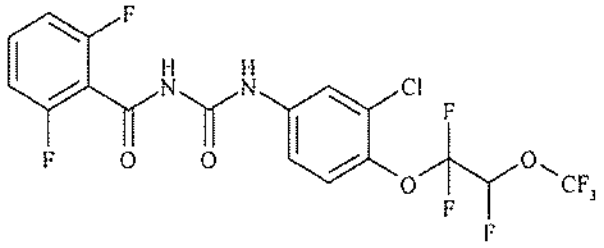
2.2 Label Recommendations

The proposed labels are adequate to allow evaluation of the residue data relative to the proposed new spot-on uses on dogs and use in cattle and poultry operations and horse barns to control stable flies and litter beetles. No label updates are required at this time.

3.0 Introduction

3.1 Chemical Identity

Table 3.1. Novaluron Nomenclature.

Chemical structure	
Common name	Novaluron
IUPAC name	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-[2,6-difluorobenzoyl]urea
CAS name	*N*-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide
CAS registry number	116714-46-6
End-use products (EPs)	CSI Fipronil + Novaluron (EPA Reg. No. 53883-NEW; 20% novaluron); Novaluron® 0.2G (EPA Reg. No. 53883-xxx; 0.2% novaluron)

3.2 Physical/Chemical Characteristics

Novaluron, a benzoylphenyl urea compound, is a pesticide chemical belonging to the class of insecticides called IGRs. IGRs kill the insects over a period of a few days by disrupting the normal growth and development of immature insects. Novaluron acts as an insecticide mainly by ingestion, but has some contact activity. It has a low vapor pressure (1.2×10^{-7} mm Hg) and appears to be immobile in soils according to the McCall classification (McCall *et al.*, 1980). A table of the physicochemical properties can be found in Appendix B.

3.3 Pesticide Use Pattern

CSI has submitted a draft label for CSI Fipronil + Novaluron (EPA Reg. No. 53883-NEW) to include the proposed new spot-on uses (Table 3.3.1) on dogs and a draft label for Novaluron® 0.2G (EPA Reg. No. 53883-xxx) to include the proposed new use in cattle and poultry operations and horse barns to control stable flies and litter beetles (Table 3.3.2).

Tolerances are not required based on the proposed new uses. Additionally, the proposed cattle and poultry operation and horse barn uses are not expected to contribute to livestock dietary burdens, so revised livestock tolerances are not required. Tolerances for residues of novaluron are established under 40 CFR §180.598 in/on a wide variety of crops at levels ranging from 0.05 to 50 ppm. Tolerances for residues of novaluron are also established in/on the following livestock commodities: eggs, milk, milk fat, and the meat, fat, kidney, liver, and meat byproducts (except kidney and liver) of cattle, goat, horse, sheep, poultry, and hog. Additionally, novaluron is registered for use in food and feed handling establishments, and a tolerance of 0.01 ppm has been established for residues in/on food and feed commodities other than those covered by a higher tolerance as a result of use on growing crops. A time-limited tolerance of 0.50 ppm for residues of novaluron in/on strawberry that expired on 31-DEC-2011 is included in 40 CFR §180.598(b). HED has recommended that this tolerance be deleted since it is expired and superseded by the established tolerance of 0.45 ppm for residues of novaluron in/on berry, low growing, subgroup 13-07G, except lowbush blueberry.

Table 3.3.1. Summary of Proposed Use Directions for the Novaluron Spot-On Use.

EPA Reg. No.	Use Site	Application Rate (per dog)	Use Restrictions
53883-NEW	Small dogs up to 22 lbs	0.67 ml (0.023 fl. oz applicator tube) 0.14 mg ai/treatment	For control of fleas and ticks on dogs and puppies 8 weeks of age and older. Do not use on puppies under 8 weeks in age. Use entire contents of tube on each dog. Monthly application is recommended for effective control of fleas and ticks and to prevent infestation. Do not reapply for 30 days (4 weeks). Apply as a spot-on to the dog's back between the shoulder blades from the back of the neck to a point midway between the neck and tail. Do not use multiple tubes on one dog.
	Medium dogs from 23 to 44 lbs	1.34 ml (0.045 fl. oz applicator tube) 0.28 mg ai/treatment	
	Intermediate dogs from 45 to 88 lbs	2.68 ml (0.091 fl. oz applicator tubes) 0.567 mg ai/treatment	
	Large dogs from 89 to 132 lbs	4.02 ml (0.136 fl. oz applicator tubes) 0.85 mg ai/treatment	

Table 3.3.2. Summary of Proposed Use Directions for Use in Cattle and Poultry Operations and Horse Barns.

[EPA File Symbol], Name, and Formula Type	Use Sites and Application Timing	Appl. Method & Timing	Max. Single Appl. Rate (lb ai/A)[2]	Max. Seasonal Appl. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations[1]
[53883-xxx], Novaluron® 0.2G, Granules 0.2% novaluron (ai)	Cattle Operations	Hand Dispersal, Belly Grinder, Cup, Rotary Spreader, Spoon	0.8 (0.00002 lb ai/ft^2)	Not provided	NA	Apply directly to stable fly breeding sites such as stray around bales or in stay around dairy barns and all other premise areas where stable flies breed.
	Poultry Operations		1.6 (0.00004 lb ai/ft^2)			Treat the entire manure area approximately one week after manure removal. Repeat treatment after each removal or when beetle larvae are found.
	Horse Barns		0.8 (0.00002 lb ai/ft^2)			Treat the entire area approximately 1 week after manure removal. Repeat treatment after each removal or when beetle larvae are found.

[1] The following restrictions are included on the draft label:

a) Do not apply Novaluron® 0.2G directly to livestock or livestock feed as illegal residues may result.
b) Do not feed manure treated with Novaluron® 0.2G to animals.
c) To avoid illegal residues, allow 1 day (24 hours) between last application and slaughter.
d) Manure treated with Novaluron® 0.2G may be used as a soil fertilizer supplement. Do not apply more than 4 tons of manure treated with Novaluron® 0.2G per acre per year. Do not apply treated manure to small grain crops that will be harvested or grazed, or illegal residues may result.

[2] lb ai/ft[2] provided by CSI in MRID 49085601.

3.4 Anticipated Exposure Pathways

RD has requested an assessment of human-health risk to support the CSI-proposed new uses of novaluron as a dog spot-on and to control stable flies and litter beetles in cattle and poultry operations and horse barns. Humans may be exposed to novaluron in food and drinking water, since novaluron may be applied directly to growing crops and application may result in novaluron reaching surface and ground water sources of drinking water. Adults and children may be exposed to novaluron in residential settings due to the proposed and registered uses. In an occupational setting, applicators may be exposed while handling the pesticide prior to application, as well as during application.

This risk assessment considers all of the aforementioned exposure pathways based on the proposed new uses of novaluron, but also considers the existing registered uses for the dietary and residential exposure assessments.

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (http://www.hss.energy.gov/nuclearsafety/env/guidance/justice/eo12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture (USDA) under the National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA; 2003-2008) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

4.1 Toxicology Studies Available for Analysis

The hazard database for novaluron is adequate for risk assessment. On March 15, 2012, the Hazard and Science Policy Council (HASPOC) concluded, based on a weight-of-evidence (WOE) approach, that a subchronic inhalation toxicity study was not required (TXR# 0052351). This approach considered all of the available hazard and exposure information for novaluron. However, this study may be necessary to support future uses. Additionally, a guideline immunotoxicity study has been submitted and reviewed by the Agency (MRID 48690105).

4.2 Absorption, Distribution, Metabolism, and Excretion (ADME)

Novaluron exhibited marginal oral absorption (16-18%), and absorption appeared to be saturated for the high dose. Peak plasma concentrations occurred at 2-5 hours. The most prevalent urinary metabolite was 2, 6-difluorobenzoic acid. Other components individually represented no more than 5.9% of the dose and most represented considerably less than 1%. Quantitatively, fecal metabolites accounted for <2% of the dose. In the repeated-dose group, some tissues such as fat contained measurable radioactivity at 168 hours post dose, but did not appear to suggest significant potential for bioaccumulation or sequestration at the doses tested. Biliary contribution for fecal excretion appears to be insignificant. Excretion was relatively rapid and was complete within 48 hours primarily via the feces and to a lesser extent via urine in rat.

4.3 Toxicological Effects

Novaluron was categorized as having low acute toxicity via the oral (Toxicity Category IV), dermal (Toxicity Category III) and inhalation routes (Toxicity Category IV). No ocular (Toxicity Category IV) or dermal irritation (Toxicity Category IV) was noted. Novaluron is not a dermal sensitizer.

In subchronic and chronic toxicity studies, novaluron's primary effects were on the hematopoietic system. These effects do not appear to worsen with time, and included methemoglobinemia, decreased hemoglobin, decreased hematocrit, decreased RBCs (or erythrocytes), and increased reticulocyte counts that were associated with compensatory erythropoiesis. Increased spleen weights and/or hemosiderosis in the spleen were considered to be due to enhanced removal of damaged erythrocytes and not to a direct immunotoxic effect.

There was no maternal or developmental toxicity seen in the rat and rabbit developmental toxicity studies up to the limit doses. In the two-generation reproductive toxicity study in rats, both parental and offspring toxicity (increased spleen weights) were observed at the same dose. Reproductive toxicity (decreases in epididymal sperm counts and increased age at preputial separation in the F_1 generation) was observed at a higher dose than the increased spleen weights and were consistent with the primary effects in the database.

There were no adverse effects observed in the 28-day dermal study in rats up to the limit dose.

Clinical signs of neurotoxicity (piloerection, irregular breathing), changes in functional observational battery parameters (increased head swaying, abnormal gait), and neuropathology (sciatic and tibial nerve degeneration) were seen in the rat acute neurotoxicity study at the limit dose. However, no signs of neurotoxicity or neuropathology were observed in the subchronic neurotoxicity study in rats at similar doses or in any other subchronic or chronic toxicity study in rats, mice, or dogs.

In the submitted immunotoxicity study, the only sign of potential immunotoxicity for novaluron was a decreased anti-SRBC response at twice the limit dose in female rats.

There was no evidence of carcinogenic potential in either the rat or the mouse carcinogenicity studies. There was no concern for genotoxicity or mutagenicity. Therefore, novaluron was classified as "not likely to be carcinogenic to humans."

4.4 Safety Factor for Infants and Children (FQPA Safety Factor)

The RAB1 risk assessment team concluded that the FQPA SF could be reduced to 1X based on the following considerations outlined in more detail in the sections below: 1) the toxicology database for novaluron is adequate for risk assessment; 2) novaluron is not considered neurotoxic; 3) there is no evidence of increased susceptibility; and 4) the exposure databases are sufficient and are unlikely to underestimate exposure.

4.4.1 Completeness of the Toxicology Database

The toxicology database for novaluron is adequate for quantification of risk for dietary, residential, and occupational uses and FQPA SF evaluation. The following acceptable studies are available for evaluation: developmental toxicity studies in rats and rabbits, a two-generation reproduction study in rats, and acute and subchronic neurotoxicity studies in rats.

4.4.2 Evidence of Neurotoxicity

Acute and subchronic neurotoxicity screening batteries were performed with novaluron in rats. Novaluron is not considered neurotoxic, since effects observed in the acute neurotoxicity study were observed at the limit dose only and were not reproduced at similar, repeated doses in the subchronic neurotoxicity study. In addition, no evidence of neuropathology was observed in subchronic and chronic toxicity studies in rats, mice, or dogs.

4.4.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

There is no evidence of increased susceptibility in the rat or rabbit developmental toxicity studies up to the limit dose or in the two-generation reproduction study in rats. There are low concerns and residual uncertainties for pre- and/or postnatal toxicity.

4.4.4 Residual Uncertainty in the Exposure Database

The most recent chronic dietary food exposure assessment utilized average field trial residues, tolerance-level residues for proposed commodities, ARs for meat, milk, hog, and poultry commodities, average PCT data for apples, cabbage, cauliflower, cotton, pears, potatoes, strawberries, and tomatoes, and PCTn data for grain sorghum and sweet corn. For the remaining food commodities, 100% CT was assumed. Empirical processing factors for apple juice (translated to pear and stone fruit juice), cottonseed oil, dried plums, and tomato paste and purée, and DEEM (ver. 7.81) default processing factors for the remaining processed commodities were also used. The registered food handling use was also incorporated into the dietary assessment. All exposure and risk estimates were not of concern.

The dietary drinking water assessment utilized water concentration values generated by the Tier II Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS) model and

the Tier 1 FQPA Index Reservoir Screening Tool (FIRST) model. The resulting screening-level estimated drinking water concentrations (EDWCs) provide conservative, health-protective, high-end estimates of water concentrations which will not likely be exceeded.

The residential handler and post-application exposure assessments are based upon the residential Standard Operating Procedures (SOPs). The residential SOPs are based upon reasonable worst-case assumptions and are not expected to underestimate risk. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to novaluron.

4.5 Toxicity Endpoint and Point of Departure Selections

4.5.1 Dose-Response Assessment

Acute Dietary Endpoint: The acute reference dose (aRfD) for the general U.S. population, including infants and children, was not established since an endpoint of concern attributable to a single dose was not identified. In the acute neurotoxicity study, neurotoxic signs and neuropathology were seen only at 2000 mg/kg (limit dose) with a relatively high no-observed adverse-effect level (NOAEL; 650 mg/kg) and no developmental toxicity was seen at the limit dose in either rat or rabbit pre-natal developmental toxicity studies.

Chronic Dietary Endpoint: The chronic reference dose (cRfD) of 0.011 mg/kg/day was determined on the basis of the chronic/carcinogenicity study in rats. The lowest-observed adverse-effect level (LOAEL) of 30.6 mg/kg/day is based on evidence of erythrocyte damage and turnover resulting in a regenerative anemia. This study provides the most protective point of departure in the hazard database with a NOAEL of 1.1 mg/kg/day. A total uncertainty factor (UF) of 100X (10X for interspecies extrapolation, 10X for intra species variability, and a 1X FQPA SF) was applied to the NOAEL of 1.1 mg/kg/day. Therefore, the cPAD is 0.011 mg/kg/day. This study is appropriate for the duration of exposure and is protective of the general U.S. population.

Incidental Oral Endpoints for All Durations: The point of departure chosen for all incidental oral scenario durations is based on the NOAEL of 4.38 mg/kg/day from the 90-day feeding study in rats. The LOAEL is 8.64 mg/kg/day based upon clinical chemical effects (decreased hemoglobin, hematocrit, and RBC counts) and changes in histopathology (increased hematopoiesis and hemosiderosis in spleen and liver). The LOC is 100 (10X for interspecies extrapolation and 10X for intra species variability and an FQPA SF of 1X). This study is protective of the offspring effects observed in the two-generation reproductive study and is thus protective of infants and children in residential settings.

Dermal Endpoint for All Durations: No adverse dermal or systemic effects were observed in the 28-day dermal study in rats; therefore, a short-term dermal endpoint was not selected. The dermal study specifically looked for blood effects, the target for novaluron, and there were no treatment related effects up to the limit dose. Although dermal endpoints were previously selected for the intermediate- and long-term scenarios, the toxicity profile for novaluron does not show progression of toxicity with increased duration. Furthermore, there is no concern for susceptibility since no effects were observed in the developmental or reproduction toxicity studies in rats or rabbits. Therefore, there is no concern for any duration of dermal exposure and no dermal endpoints are required.

Inhalation Endpoints for All Durations: Similar to the incidental oral endpoint, the POD chosen for all inhalation scenario durations is based on the NOAEL of 4.38 mg/kg/day from the 90-day feeding study in rats. The LOAEL is 8.64 mg/kg/day based upon clinical chemical effects (decreased hemoglobin, hematocrit, and RBC counts) and changes in histopathology (increased hematopoiesis and hemosiderosis in spleen and liver). The LOC for residential and occupational exposures are for MOEs <100 (similar to the intermediate-term dermal endpoint). This study is protective of children and adults in residential settings, as well as workers in occupational settings.

4.5.2 Recommendation for Combining Routes of Exposures for Risk Assessment

Based upon common effects and the use of an oral 90-day study in rats for the incidental oral and inhalation routes, these exposures can be combined for all residential scenarios for all durations. Since there are no dermal endpoints for novaluron, dermal exposures do not need to be combined with inhalation exposures for residential and occupational assessments.

4.5.3 Cancer Classification and Risk Assessment Recommendation

In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), novaluron is classified as "not likely to be carcinogenic to humans" based on the lack of evidence for carcinogenicity in mice and rats (TXR# 0052361).

4.5.4 Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for Novaluron for Use in Dietary and Non-Occupational Human-Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population, including Infants and Children)	None	None	None	An endpoint of concern attributable to a single dose was not identified. An acute RfD was not established.
Chronic Dietary (All Populations)	NOAEL = 1.1 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	Chronic RfD = 0.011 mg/kg/day cPAD = 0.011 mg/kg/day	Combined chronic toxicity/carcinogenicity feeding in rat LOAEL = 30.6 mg/kg/day based on erythrocyte damage resulting in a compensatory regenerative anemia.
Incidental Oral, All Durations	NOAEL = 4.38 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	Residential LOC for MOE <100	90-day feeding study in rat LOAEL = 8.64 mg/kg/day based on clinical chemistry (decreased hemoglobin, hematocrit, and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for Novaluron for Use in Dietary and Non-Occupational Human-Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Dermal, All Durations	A short-term dermal endpoint was not selected since there were no adverse dermal or systemic effects observed in the 28-day dermal study in rats. The dermal study specifically looked for blood effects, the target for novaluron, and there were no treatment related effects up to the limit dose. Although dermal endpoints were previously selected for the intermediate- and long-term scenarios, the toxicity profile for novaluron does not show progression of toxicity with increased duration. Furthermore, there is no concern for susceptibility since no effects were observed in the developmental or reproduction toxicity studies in rats or rabbits. Therefore, there is no concern for any duration of dermal exposure and no dermal endpoints are required.			
Inhalation, All Durations	NOAEL = 4.38 mg/kg/day (inhalation-absorption rate = 100%)	UF_A = 10X UF_H =10X FQPA SF = 1X	Residential LOC for MOE <100	90-day feeding study in rat LOAEL = 8.64 mg/kg/day based on clinical chemistry (decreased hemoglobin, hematocrit, and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
Cancer (oral, dermal, inhalation)	Classification: Not likely to be carcinogenic to humans.			

Point of departure = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population-adjusted dose (c = chronic). RfD = reference dose. LOC = level of concern. MOE = margin of exposure.

Table 4.5.4.2. Summary of Toxicological Doses and Endpoints for Novaluron for Use in Occupational Human-Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Dermal, All Durations	A short-term dermal endpoint was not selected since there were no adverse dermal or systemic effects observed in the 28-day dermal study in rats. The dermal study specifically looked for blood effects, the target for novaluron, and there were no treatment related effects up to the limit dose. Although dermal endpoints were previously selected for the intermediate- and long-term scenarios, the toxicity profile for novaluron does not show progression of toxicity with increased duration. Furthermore, there is no concern for susceptibility since no effects were observed in the developmental or reproduction toxicity studies in rats or rabbits. Therefore, there is no concern for any duration of dermal exposure and no dermal endpoints are required.			
Inhalation, All Durations	NOAEL = 4.38 mg/kg/day (inhalation-absorption rate = 100%)	UF_A = 10X UF_H =10X	Occupational LOC for MOE <100	90-day feeding study in rat LOAEL = 8.64 mg/kg/day based on clinical chemistry (decreased hemoglobin, hematocrit, and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
Cancer (oral, dermal, inhalation)	Classification: Not likely to be carcinogenic to humans.			

Point of departure = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. UF =

uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). MOE = margin of exposure. LOC = level of concern.

5.0 Dietary Exposure and Risk Assessment

5.1 Food Residue Profile

An overview of the residues of concern can be found in the previous risk assessment (Memo, J. Van Alstine, *et al.*, 15-MAY-2013).

No new residue chemistry data were submitted for the use of novaluron in cattle and poultry operations and horse barns to control stable flies and litter beetles. The registration request originally came in as a non-food use. The request was brought to the Science Advisory Council for Chemistry (ChemSAC), and the ChemSAC determined that the proposed use is a food use; however, rotational crop studies and agricultural premise use studies in cattle and poultry are not required at this time (ChemSAC Minutes 24-APR-2013).

The proposed use is considered a food use for the following reasons: 1) livestock may be exposed to novaluron based on the proposed use pattern; and 2) novaluron-treated manure may be spread on fields where food crops are grown. Although the proposed use is a food use, agricultural premise use studies in cattle and poultry, as per Guideline 860.1480, are not required at this time for the following reasons: 1) the established meat, milk, poultry, and egg tolerances are based on reasonably balanced dietary burdens (RBDBs) of 16.9 ppm for beef cattle, 11.9 ppm for dairy cattle, 2.4 ppm for poultry, and 2.5 ppm for swine, and the proposed uses to control stable flies and litter beetles are not expected to contribute significantly to the livestock dietary burdens; and 2) given the proposed application instructions and product formulation (granular), livestock dermal exposure to novaluron is expected to be insignificant from the proposed use. Additionally, a rotational crop study, per Guideline 860.1850, that simulates the maximum amount of manure that can be applied to a field is also not required at this time for the following reasons: 1) crops are not likely to have quantifiable residues due to the application of novaluron-treated manure to fields; 2) the available rotational crop field trials indicate that residues are not likely to be taken up and the plant metabolism studies indicate that novaluron is not readily translocated through leaves; 3) novaluron has a fairly short half-life; and 4) using a conservative calculation, the "application rate" of novaluron was calculated to be 0.053 lb ai/A due to the use of treated manure on fields. This "application rate" is below the limited field rotational crop study application rate of 0.24 lb ai/A (equivalent to 4.5X) that resulted in residues <0.05 ppm, and the confined rotational crop study application rate of 0.089 lb ai/A (equivalent to 1.7X) that resulted in residues <0.005 ppm.

Since the proposed uses in cattle and poultry operations and horse barns are not expected to result in significant livestock dietary or dermal exposures in comparison to the residues resulting from the currently registered uses, revised livestock tolerances are not required. Additionally, crops are not likely to have quantifiable residues due to the application of novaluron-treated manure to fields, so tolerances for indirect or inadvertent residues are not required.

Novaluron is registered for use in food- and feed-handling establishments, including uses in residential and commercial buildings and structures and their immediate surroundings, and on modes of transportation. This use was assessed in a 2011 risk assessment and a tolerance was established for residues of novaluron in/on food and feed commodities other than those covered

by a higher tolerance as a result of use on growing crops at 0.01 ppm (Memo, L. Venkateshwara, *et al.*, 15-SEP-2011; D377471). This use has been incorporated into the dietary exposure assessment.

5.2 Dietary Risk Assessment

5.2.1 Description of Residue Data Used in Dietary Assessment

The proposed uses did not result in changes to the most recent dietary exposure assessment (Memo, J. Van Alstine, D401262; 15-MAY-2013); however, for the purposes of the aggregate assessment, this information has been included in this risk assessment. A partially refined chronic dietary-exposure (food plus water) and risk assessment was recently conducted using DEEM-FCID, Version 3.16, which uses food consumption data from the USDA's NHANES/WWEIA survey from 2003 through 2008. The assessment was performed for the general U.S. population and all population subgroups. The chronic analysis incorporated recently updated average PCT and PCTn data. ARs for meat, milk, hog, and poultry commodities were calculated using average field trial residues, PCTn and PCT data, and 100% CT for some commodities. The chronic analysis also incorporated average field trial residues, tolerance-level residues for the proposed commodities, average greenhouse trial residues for tomatoes, and half-LOQ residues for food commodities other than those covered by a higher tolerance as a result of use on growing crops from the registered use in food and feed handling establishments. Additionally, empirical processing factors for apple juice (translated to pear and stone fruit juice), cottonseed oil, dried plums, and tomato paste and purée, and DEEM (ver. 7.81) default processing factors for the remaining processed commodities, where provided were incorporated. Drinking water estimates were provided by EFED in the following memorandum: "Drinking Water Assessment in Support of the New Use of Novaluron in Peanuts and Soybeans" (H. Zhong, 27-AUG-2012; D402324). The combined surface water EDWC value for novaluron, chlorophenyl urea, and chloroaniline (4.086 ppb) was directly incorporated into the assessment.

5.2.2 Percent Crop Treated Used in Dietary Assessment

A Screening Level Usage Analysis (SLUA) memorandum entitled, "Usage Report Package in Support of Novaluron (124002), BEAN DP# 407102" (C. Doucoure, 05-DEC-2012) and a PCTn memorandum entitled, "Update of Percent Crop Treated for New Use (PCTn): Novaluron (124002) Use on Sorghum and Sweet Corn" (C. Doucoure, *et al.*, 01-FEB-2013) were provided by BEAD. The market leader approach was used by BEAD to determine the PCTn values for sorghum and sweet corn.

The chronic dietary analysis incorporated average PCT data for apples (10%), cabbage (10%), cauliflower (<2.5%), cotton (<2.5%), pears (15%), potatoes (<2.5%), strawberries (35%), and tomatoes (<1%) and average PCTn data for grain sorghum (2%) and sweet corn (36%). For the remaining food commodities, 100% CT was assumed. Livestock dietary burdens of novaluron were calculated based on the proposed/registered uses, and incorporated average field trial residues, PCTn data for grain sorghum (2%) and sweet corn (36%), average PCT data for apple (10%) and cotton (<2.5%), and an assumption of 100% CT for sugarcane, AGF, and cowpea seed. These livestock dietary burdens were used, along with average transfer coefficients, to calculate anticipated secondary residues for meat, milk, hog, and poultry commodities which were incorporated into the chronic dietary assessment.

5.2.3 Acute Dietary Risk Assessment

An acute dietary assessment was not conducted for novaluron because an endpoint of concern attributable to a single dose was not identified.

5.2.4 Chronic Dietary Risk Assessment

Chronic dietary risk estimates (food and drinking water) are not of concern for the general population or any other population subgroup. The assessment was partially refined and the highest exposure and risk estimates were for the population subgroup children 1-2 years old, which utilized 55% of the cPAD for novaluron. The chronic exposure estimate for the general U.S. population utilized 14% of the cPAD. A summary table of dietary exposure and risk for novaluron can be found in Section 5.2.6. Although further refinement to the analysis is not required at this time, future assessments could be refined using additional average field trial values, additional PCT data, cooking factors, and/or monitoring data.

5.2.5 Cancer Dietary Risk Assessment

A cancer dietary assessment was not conducted because novaluron is classified as "not likely to be carcinogenic to humans."

5.2.6 Summary Table

Table 5.2.6. Summary of Chronic Dietary Exposure (Food and Drinking Water) and Risk for Novaluron.[1]

Population Subgroup	Acute Dietary		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	N/A	N/A	0.001596	14	N/A	N/A
All Infants (<1 year old)			0.002389	22		
Children 1-2 years old			**0.006033**	**55**		
Children 3-5 years old			0.004020	36		
Children 6-12 years old			0.002505	23		
Youth 13-19 years old			0.001340	12		
Adults 20-49 years old			0.001164	11		
Adults 50-99 years old			0.001213	11		
Females 13-49 years old			0.001154	11		

[1] Population with the greatest exposure is in bold.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

A residential exposure assessment was provided in a HED memorandum dated 21-MAY-2013 (L. Venkateshwara; D410803). Residential handler and post-application exposures are anticipated from the proposed use of the novaluron dog spot-on product. In assessing these exposures, the *Health Effects Division's (HED) 2012 Standard Operating Procedures (SOPs) for Residential Pesticide Exposure Assessment: Treated Pets*[1] was used. Some of the data included in the 2012 Treated Pet SOP are proprietary and, thus, are subject to the data protection provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The proposed use to control stable flies and litter beetles in cattle and poultry operations and horse barns will

[1] http://www.epa.gov/pesticides/science/residential-exposure-sop.html

not result in residential exposures since the product will not be applied by homeowners or by commercial applicators in residential settings.

There are existing residential uses of novaluron that were reassessed in April 2013[2] and are summarized here to reflect updates to HED's 2012 Residential SOPs (http://www.epa.gov/pesticides/science/residential-exposure-sop.html) along with policy changes for body-weight assumptions. Novaluron is registered for both indoor and outdoor applications to control crickets in residential and commercial buildings and structures and their immediate surroundings and on modes of transportation (Memo, L. Venkateshwara, 25-JAN-2011; D378634). Only the indoor use was assessed as this is believed to result in a greater risk potential than the outdoor perimeter treatment which is only for areas that adults and children would not contact regularly, such as around window frames and doors. This use results in the highest short-term adult and children residential exposures, and the MOEs are provided in Section 6.3.

6.1 Residential Handler Exposure

Novaluron is proposed for residential use as a spot-on for dogs. CSI Fipronil + Novaluron is proposed as a monthly topical solution for continuous protection against fleas, ticks, flea eggs, flea larvae (mosquitoes), and chewing lice. The spot-on product is designed to be self-contained as it is applied directly from the tube to the pet with the tip of the applicator used to part the pet's hair.

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are addressed somewhat differently by HED as homeowners are assumed to complete all elements of an application without use of any protective equipment.

Residential handler dermal and inhalation exposures are expected to occur from the proposed novaluron spot-on product when applied to dogs; however, quantitative assessments were not conducted for the following reasons: 1) no dermal hazard was identified; and 2) inhalation exposure is considered negligible for the application of spot-on products.

6.2 Post-Application Exposure

There is the potential for post-application exposure for individuals exposed as a result of contacting a dog previously treated with the proposed novaluron spot-on product. The quantitative exposure/risk assessment for residential post-application exposures is based on the following scenario:

- Post-application incidental oral exposure (children 1 to <2 years old only) from contacting dogs treated with novaluron.

Because no dermal hazard has been identified for novaluron, only incidental oral exposures were assessed. The lifestages selected for each post-application scenario are based on an analysis

[2] L. Venkateshwara. *Novaluron. Occupational and Residential Exposure Assessment for a Proposed Use on Peanuts and Soybeans and a Reevaluation of Existing Residential Uses with the Updated Residential SOPs) to reflect updates to HED's 2012 Residential SOP.* 30-APR-2013; D401261.

provided as an Appendix in the 2012 Residential SOPs[3]. These lifestages are not the only ones that could be potentially exposed for these post-application scenarios; however, the assessment of these lifestages is health protective for the exposures and risk estimates for any other potentially exposed lifestages.

Current HED policy requires assessment of short-, intermediate-, and long-term exposures from pet spot-on products due to the preventative nature of pet products and the potential from extended usage in more temperate parts of the country; therefore, this assessment has considered all durations of exposure.

A series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the 2012 Residential SOPs. The 2012 Residential SOP for treated pets recommends assessment of post-application exposures using day of application (i.e., Day 0) residue transfer, which is defined as a fraction of the application rate (F_{AR}). If chemical-specific transferable-residue measurements are not available, then a standard value for the F_{AR} for transfer is used. No exposure data were submitted in support of the proposed novaluron spot-on product; therefore, HED used the screening-level F_{AR} point estimate (0.02), as recommended in the 2012 Residential SOPs, to assess post-application incidental oral exposure.

The short-, intermediate-, and long-term incidental oral MOEs for children 1 to <2 years old from exposure to the proposed novaluron pet spot-on product are provided in Table 6.2. None of the exposure estimates are of concern for any sized dog (all MOEs ≥20,000).

Table 6.2. Residential Post-Application Non-Cancer Exposure and Risk Estimates from the Proposed Novaluron Spot-On Product: All Durations (Day-0 F_{AR}).

Lifestage	Post-application Exposure Scenario		Application Rate (mg ai)[1]	Dose (mg/kg/day)[2]	MOEs[3]
	Use Site	Route of Exposure			
Children 1 to <2 Years Old	Dog Spot-on	Incidental Oral	0.14 (small)	0.000141	31,000
			0.28 (medium)	0.00017	26,000
			0.567 (intermediate)	0.00022	20,000
			0.85 (large)	0.00021	20,000

[1] Based on proposed label (Reg. No. 53883-NEW).

[2] Hand-to-Mouth Dose = [(Hand Residue Loading (mg/cm^2) × Fraction of Hand Mouthed (0.13) × Surface Area of 1 Hand (150 cm^2) × Exposure Time (1.5 hrs/day) × # of Replenishment Intervals/hr (1 int/hr) × (1-((1-Saliva Extraction Factor (0.5))^(Number of Hand-to-Mouth Events per Hour (13.9 events/hr)) ÷ (# of Replenishment Intervals/hr))] / Body Weight (11 kg child 1 to <2 years old years old)].

[3] MOE = Incidental Oral POD (mg/kg/day) / Dose (mg/kg/day).

6.3 Summary of Residental Exposure as a Result of the Registered Uses

Table 6.3 summarizes the residential exposures and risk estimates for the previously assessed and registered crack and crevice use of novaluron to control crickets (Memo, L. Venkateshwara, 30-APR-2013; D401261). All residential handler and post-application scenarios resulted in MOEs greater than 100 and are not of concern to HED.

[1] Available: http://www.epa.gov/pesticides/science/residential-exposure-sop.html

Table 6.3. Summary of Residential Exposure/Risk Estimates from Registered Novaluron Uses.

Use	Exposure Scenario				Dose (mg/kg/day)	Short-Term MOE	Source
Indoor crack and crevice / spot treatment	Residential Handler Inhalation	Mixing/loading/applying wettable powders with low-pressure handwand			0.00014	3,200	D401261
		Applying ready-to-use formulations with trigger-pump sprayer			0.0000076	570,000	
	Post-application Inhalation	Adults			0.000049	89,000	
		Children (1 to <2 years old)			0.00021	21,000	
	Post-application Incidental Oral	Crack and Crevice	Carpet	Children (1 to <2 years old)	0.00059	7,400	
			Hard surfaces		0.000196	22,000	
		Spot	Carpet		0.00288	1,500	
			Hard surfaces		0.00096	4,600	

6.4 Residential Risk Estimates for Use in Aggregate Assessment

Table 6.4 reflects the residential risk estimates that are recommended for use in the aggregate assessment for novaluron. The indoor use of novaluron as a crack and crevice use results in higher short-term exposures than the proposed pet spot-on use; therefore, the crack and crevice use scenarios are recommended for the short-term aggregate assessment (see the April 2013 memo[4]). The only intermediate- and long-term residential exposures are from the proposed dog spot-on use; therefore, the proposed pet spot-on use scenarios are recommended for intermediate-term and long-term aggregate assessment.

- The recommended residential exposure for use in the short-term adult aggregate assessment reflects inhalation exposure from both indoor and outdoor applications via a low-pressure handwand.
- The recommended residential exposure for use in the short-term children 1 to <2 years old aggregate assessment reflects inhalation and hand-to-mouth exposures from post-application exposure to indoor applications
- The recommended residential exposure for use in the intermediate- and long-term children 1 to <2 years old aggregate assessment reflects post-application hand-to-mouth exposures from the dog spot-on use.

[4] L. Venkateshwara. *Novaluron. Occupational and Residential Exposure Assessment for a Proposed Use on Peanuts and Soybeans and a Reevaluation of Existing Residential Uses with the Updated Residential SOPs) to reflect updates to HED's 2012 Residential SOP.* 30-APR-2013, D401261.

Table 6.4. Recommendations for the Residential Exposures for the Novaluron Aggregate Assessment.[1]

Lifestage	Residential Handler						Residential Post-application							
	Dose (mg/kg/day)[2]			MOE[3]			Dose (mg/kg/day)[4]				MOE[5]			
	Dermal	Inhalation	Total	Dermal	Inhalation	Total	Dermal	Inhalation	Oral	Total	Dermal	Inhalation	Oral	Total
Short-Term														
Adult	NA	0.00014	0.00014	NA	3,200	3,200	N/A	0.000049	N/A	0.000049	NA	89,000	N/A	89,000
Child	N/A						N/A	0.00021	0.00288	0.0031	NA	21,000	1,500	1,400
Intermediate- and Long-Term														
Adult Male	N/A						N/A	NA	N/A	NA	N/A	NA	N/A	N/A
Child							N/A	N/A	0.00022	0.00022	N/A	N/A	20,000	20,000

[1] Bolded risk estimates should contribute to the residential exposure portion of the aggregate assessment.
[2] Residential Handler Dose = the highest handler dose for each applicable lifestage of all scenarios assessed (see Table 6.3). Total = inhalation only.
[3] Residential Handler MOE = the MOEs associated with the highest doses identified (see Table 6.3). Total = Inhalation MOE only.
[4] Residential Post-application Dose = the highest post-application dose for each applicable lifestage of all scenarios assessed (see Tables 6.2 and 6.3). Total = inhalation + incidental oral, where applicable.
[5] Residential Post-application MOE = the MOEs associated with the highest doses identified (see Tables 6.2 and 6.3). Total = 1/((1/Inhalation MOE) + (1/Incidental oral MOE)) where applicable.

7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure. In the case of novaluron, aggregate risk assessments were performed for short-term aggregate exposure (food + drinking water + residential) and intermediate-term aggregate exposure (food + drinking water + residential). Even though there are long-term residential exposures, the intermediate-term aggregate assessment is protective of chronic aggregate exposure since there is no progression of effects in the database and there is only one POD for all durations of incidental oral exposure. An acute aggregate assessment was not conducted for novaluron because an endpoint of concern attributable to a single dose was not identified. Additionally, a cancer aggregate assessment was not conducted because novaluron was classified as "not likely to be carcinogenic to humans." All potential exposure pathways were assessed in the aggregate risk assessment.

7.1 Short-Term Aggregate Risk

Short-term (1- to 30-day) aggregate risk assessments are necessary for both adults and children since there is potential for both short-term handler exposure and short-term post-application exposure from the residential uses of novaluron. For the short-term aggregate risk assessment, potential residential exposures were combined with food and drinking water exposures. A short-term dermal endpoint has not been selected for novaluron; therefore, the short-term adult and child aggregate risk estimates do not include dermal exposures. Specifically, the short-term aggregate assessment for adults combines dietary exposures with handler inhalation exposures resulting from the indoor crack and crevice uses. For young children, the short-term aggregate assessment combines dietary exposure with potential post-application inhalation and incidental oral exposure (from hand-to-mouth contact with treated surfaces) resulting from the indoor uses. See Table 6.4 for more information on the residential risk estimates that are recommended for use in the aggregate assessment for novaluron.

The short-term residential exposure estimates were aggregated with the chronic dietary (food + drinking water) to provide a worst-case estimate of short-term aggregate risk for the U.S. population and children 1-2 years old (the child population subgroup with the highest estimated chronic dietary food + drinking water exposure). As the short-term aggregate MOEs are greater than 100, risk estimates do not exceed HED's LOC.

Table 7.1. Short-Term Aggregate Risk Calculations for Novaluron.

Population Subgroups	Short-Term Scenario[1]					
	NOAEL (mg/kg/day)	LOC[2]	Max Exposure[3] (mg/kg/day)	Average Dietary Exposure (mg/kg/day)	Residential Exposure[4] (mg/kg/day)	Aggregate MOE (dietary and residential)[5]
Adult	4.38	100	0.0438	0.001596	0.00014	2500
Children 1-2 years old	4.38	100	0.0438	0.006033	0.0031	480

[1] A short-term dermal endpoint has not been selected for novaluron; therefore dermal exposure was not included in the short-term aggregate assessment.
[2] The LOC (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.
[3] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE.
[4] Residential Exposure = Handler Inhalation Exposure for Adults and [Post-application Oral Exposure + Post-application Inhalation Exposure] for Children.

[5] Aggregate MOE = [NOAEL ÷ (Avg. Dietary Exposure + Residential Exposure)].

7.2 Intermediate-Term and Chronic Aggregate Risk

Intermediate-term (1- to 6-months) and chronic (>6 months) aggregate risk assessments are necessary since there is the potential for intermediate-term and long-term post-application exposure from the proposed dog spot-on use of novaluron. Since there is no progression of effects in the toxicology database and there is only one POD for all durations of incidental oral exposure, the intermediate-term aggregate assessment is protective of chronic/long-term aggregate exposure.

For the intermediate-term aggregate risk assessment, potential residential exposures were combined with food and drinking water exposures. An intermediate-term dermal endpoint has not been selected for novaluron, and inhalation exposure is considered negligible for the application of spot-on products; therefore, the intermediate-term aggregate risk estimates do not include dermal and inhalation exposures. For young children, the intermediate-term aggregate assessment combines dietary exposure with potential post-application incidental oral exposure (from hand-to-mouth contact with treated pets) resulting from the dog spot-on use. For adults, since there is no dermal endpoint and inhalation exposure is expected to be negligible, the average dietary consumption (food + drinking water) exposure estimate is representative of intermediate-term aggregate risk. See Table 6.4 for more information on the residential risk estimates that are recommended for use in the aggregate assessment for novaluron.

The intermediate-term indoor residential exposure estimates were aggregated with the chronic dietary (food+ drinking water) to provide a worst-case estimate of intermediate-term aggregate risk for adults and children 1-2 years old (the child population subgroup with the highest estimated chronic dietary food + drinking water exposure). As the intermediate-term aggregate MOEs are greater than 100, risk estimates do not exceed HED's LOC. The intermediate-term aggregate risk assessment is protective of chronic/long-term aggregate exposure.

Table 7.2. Intermediate-Term and Chronic Aggregate Risk Calculations for Novaluron.

Population Subgroups	Intermediate-Term Scenario[1]					
	NOAEL (mg/kg/day)	LOC[2]	Max Exposure[3] (mg/kg/day)	Average Dietary Exposure (mg/kg/day)	Residential Exposure[4] (mg/kg/day)	Aggregate MOE (dietary and residential)[5]
Adult	4.38	100	0.0438	0.001596	N/A	2,700
Children 1-2 years old	4.38	100	0.0438	0.006033	0.00022	700

[1] An intermediate-term dermal endpoint has not been selected for novaluron, and inhalation exposure is considered negligible for the application of spot-on products; therefore, the intermediate-term aggregate risk estimate does not include dermal and inhalation exposures.

[2] The LOC (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.

[3] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE.

[4] For adults, since there is no dermal endpoint and inhalation exposure is expected to be negligible, there is no residential exposure estimate to combine with dietary exposures. For children, Residential Exposure = [Incidental Oral Exposure + Dermal Exposure + Inhalation Exposure].

[5] Aggregate MOE = [NOAEL ÷ (Avg. Dietary Exposure + Residential Exposure)].

8.0 Cumulative Exposure/Risk Characterization

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to novaluron and any other substances and novaluron does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore,

EPA has not assumed that novaluron has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

9.0 Occupational Exposure/Risk Characterization

Occupational exposure assessments of the proposed uses were provided in HED memorandum dated 21-MAY-2013 (L. Venkateshwara; D410803) and 21-MAY-2013 (L. Venkateshwara; D406091).

9.1 Short-/Intermediate-Term Handler Risk

Dog Spot-On Use
For the dog spot-on use, there is the potential for occupational handler exposure (i.e., veterinarians, veterinary assistants, and groomers). However, there is no dermal toxicity related with the use of novaluron and inhalation exposures are expected to be negligible from application of the spot-on product; therefore, quantitative assessments were not conducted.

Cattle and Poultry Operations and Horse Barns Use
For the cattle and poultry operations and horse barns use, occupational handler exposure is expected. The scenarios assessed for occupational handlers include: loading/applying granules by backpack; loading/applying granules by belly grinder; loading/applying granules by cup; loading/applying granules by rotary spreader; loading/applying granules by spoon; and applying granules via hand dispersal.

It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include the Pesticide Handlers Exposure Database (PHED) 1.1, the Agricultural Handler Exposure Task Force (AHETF) database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures," are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table[5]," which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the Agency website[6].

Based on HED ExpoSAC SOP No. 9.1, the area treated in a day was assumed to be 1 acre for cattle operations, poultry operations, and horse barns. The average adult body weight of 80 kg was used for estimating inhalation dose because the selected toxicological PODs are not based on developmental effects. There is no short- or intermediate-term dermal POD. The inhalation endpoints were selected from a 90-day feeding study in the rat. Since inhalation absorption data are not available, toxicity by the inhalation route is considered to be equivalent to toxicity by the oral route of exposure.

[5] Available: http://www.epa.gov/opp00001/science/handler-exposure-table.pdf
[6] Available: http://www.epa.gov/pesticides/science/handler-exposure-data.html

HED classifies exposures from 1 to 30 days as short-term and exposures and from 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most commercial pest control, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month period; however, commercial applicators may apply a product over a period of weeks. In warm climates, flies breed year round and repeated applications of novaluron are needed to keep the fly larvae and litter beetles under control, resulting in short and intermediate-term exposures to handlers. Long-term exposure is not expected.

For pesticide handlers, it is HED's standard practice to present estimates of dermal exposure for "baseline"; that is, for workers wearing a single layer of work clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, and no protective gloves, as well as for "baseline" and the use of protective gloves or other PPE as might be necessary. For the proposed new use of novaluron granule for fly control, no PPE, except gloves, were recommended on the label.

The occupational handler short- and intermediate-term non-cancer inhalation exposure risk estimates are not of concern to HED with baseline attire (i.e., single layer of clothing, no gloves, and no respirator) for all loader/applicator scenarios. With baseline attire, the short- and intermediate-term inhalation MOEs for all loader/applicator scenarios for novaluron application ranged from 470 to 22,000.

Table 9.1. Short-and Intermediate-Term Inhalation Occupational Exposure and Risk Estimates for Novaluron. All Estimates are at Baseline Mitigation (i.e., Without a Respirator).

Exposure Scenario	Inhalation Unit Exposure (ug/lb ai)[1]	Maximum Application Rate (lb ai/A)[2]	Area Treated or Amount Handled Daily (acres)[3]	Inhalation	
				Dose (mg/kg/day)[4]	MOE[5]
Loader/Applicator					
L/A, Granular, Backpack	23.8	1.6	1	0.000476	9,200
L/A, Granular, Belly grinder	62	1.6	1	0.00124	3,500
L/A, Granular, Cup	12.5	1.6	1	0.00025	18,000
L/A, Granular, Rotary Spreader	10	1.6	1	0.0002	22,000
L/A, Granular, Spoon	121	1.6	1	0.00243	1,800
Applicator					
Applicator, Hand Dispersal	470	1.6	1	0.0094	470

[1] Based on "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (March 2012); includes data from PHED/ORETF/AHETF (level of mitigation: Baseline, PPE, Eng. Controls). The use does not fall under the worker protection standard (WPS).
[2] Based on registered or proposed label (Reg. No. #53883-xxx).
[3] Exposure Science Advisory Council Policy #9.1.
[4] Inhalation Dose =Inhalation Unit Exposure (µg/lb ai) x Conversion Factor (0.001 mg/ug) x Application Rate (lb ai/acre) x Area Treated or Amount Handled Daily (A/day) /BW (kg).
[5] Inhalation MOE = Inhalation NOAEL (mg/kg/day)/ Inhalation Dose (mg/kg/day).

9.2 Short-/Intermediate-Term Post-Application Risk

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the

type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

Dog Spot-On Use

For the proposed novaluron dog spot-on use, occupational post-application activities are expected to be significantly less than residential post-application exposures. Dogs are expected to be treated and returned to their owners such that occupational post-application contact will be negligible. As a result, no quantitative occupational post-application exposure and risk assessment has been performed. The residential post-application exposure and risk assessment (Section 6.2) is considered protective for any potential occupational post-application exposures and risks.

Cattle and Poultry Operations and Horse Barns Use

For the proposed use of novaluron to control stable fly larvae in cattle operations and horse barns, and to control litter beetles in poultry operations, there are no site-specific post-application activities performed after treatment of fly breeding areas. Therefore, a quantitative post-application assessment was not conducted for the proposed use of novaluron granules.

The proposed Novaluron® 0.2G label has no Worker Protection Standard requirements; therefore, a restricted-entry interval (REI) is not applicable for the proposed use of novaluron.

10.0 References

Previous Risk Assessments

- Van Alstine, J., *et al.*, 15-MAY-2013, D400705. Novaluron: Human-Health Risk Assessment for Proposed Section 3 Uses on Peanut and Soybean.

- Venkateshwara, L. *et al.*, 15-SEP-2011, D377471. Novaluron: Human-Health Risk Assessment for Proposed Section 3 Uses on Sweet Corn and in Food- or Feed-Handling Establishments.

- Van Alstine, J., *et al.*, 23-FEB-2010, D364307. Novaluron: Human-Health Risk Assessment for Proposed Section 3 Use on Grain Sorghum.

HASPOC Memo

- Van Alstine, J., 17-APR-2012, TXR # 0052351. Novaluron: Summary of Hazard and Science Policy Council (HASPOC) Meeting of March 15, 2012: Recommendations on the requirement of a subchronic inhalation study for novaluron.

ChemSAC Minutes

- ChemSAC Minutes 24-APR-2013

Dietary Memo

- Van Alstine, J., 15-MAY-2013, D401262. Novaluron. Chronic Dietary (Food and Drinking Water) Exposure and Risk Assessment for the Proposed Uses on Peanut and Soybean.

Drinking Water Memo

- Zhong, H., 27-AUG-2012, D402324. Drinking Water Assessment in Support of the New Use of Novaluron in Peanuts and Soybeans.

Occupational and Residential Exposure Memos

- Venkateshwara, L., 21-MAY-2013, D406091. Novaluron. Occupational and Residential Exposure Assessment for a Proposed Use to Control Stable Fly Larvae in Cattle Operations and Horse Barns, and to Control Litter Beetles in Poultry Operations.

- Venkateshwara, L., 21-MAY-2013, D410803. Novaluron: Occupational and Residential Exposure and Risk Assessment for Proposed Pet Spot-On Use.

- Venkateshwara, L., 30-APR-2013, D401261, Novaluron. Occupational and Residential Exposure Assessment for a Proposed Use on Peanuts and Soybeans and a Reevaluation of Existing Residential Uses with the Updated Residential SOPs.

- Venkateshwara, L., 25-JAN-2011, DP 378634, Novaluron Occupational and Residential Exposure/Risk Assessment for a Crack and Crevice Use.

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Appendix A. Toxicology Profile and Executive Summaries

A.1 Toxicology Data Requirements

The requirements (40 CFR 158.340) for novaluron are in Table A.1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Table A.1. Toxicology Data Requirements.

Study		Technical	
		Required	Satisfied
870.1100	Acute Oral Toxicity	Yes	Yes
870.1200	Acute Dermal Toxicity	Yes	Yes
870.1300	Acute Inhalation Toxicity	Yes	Yes
870.2400	Acute Eye Irritation	Yes	Yes
870.2500	Acute Dermal Irritation	Yes	Yes
870.2600	Skin Sensitization	Yes	Yes
870.3100	90-Day Oral Toxicity in Rodents	Yes	Yes
870.3150	90-Day Oral Toxicity in Nonrodents	No	No
870.3200	21/28-Day Dermal Toxicity	Yes	Yes
870.3250	90-Day Dermal Toxicity	No	No
870.3465	90-Day Inhalation Toxicity	No	No
870.3700a	Prenatal Developmental Toxicity (rodent)	Yes	Yes
870.3700b	Prenatal Developmental Toxicity (nonrodent)	Yes	Yes
870.3800	Reproduction and Fertility Effects	Yes	Yes
870.4100a	Chronic Toxicity (rodent)	No	No
870.4100b	Chronic Toxicity (nonrodent)	Yes	Yes
870.4200a	Carcinogenicity (rat)	No	No
870.4200b	Carcinogenicity (mouse)	No	No
870.4300	Combined Chronic Toxicity/Carcinogenicity (mice and rats)	Yes	Yes
870.5100	Mutagenicity—Bacterial Reverse Mutation Test	Yes	Yes
870.5300	Mutagenicity—Mammalian Cell Gene Mutation Test	Yes	Yes
870.5375	In vitro Mammalian Chromosomal Aberrations	Yes	Yes
870.5395	Mammalian Erythrocyte Micronucleus	Yes	Yes
870.5550	Unscheduled DNA Synthesis	Yes	Yes
870.5550	Mutagenicity–Rec assay with *Bacillus subtilis*	Yes	Yes
870.6200a	Acute Neurotoxicity Screening Battery (rat)	Yes	Yes
870.6200b	90-Day Neurotoxicity Screening Battery (rat)	Yes	Yes
870.6300	Developmental Neurotoxicity	No	No
870.7485	Metabolism and Pharmacokinetics	Yes	Yes
870.7600	Dermal Penetration	Yes	Yes
870.7800	Immunotoxicity	Yes	Yes

A.2 Toxicity Profiles

Table A.2.1. Acute Toxicity of Novaluron.

Guideline No.	Study Type	MRID #(s)	Results	Toxicity Category
870.1100 (81-1)	Acute Oral (rat)	44961001	LD_{50} >5000 mg/kg	IV
870.1200 (81-2)	Acute Dermal (rat)	45003201	LD_{50} >2000 mg/kg	III
870.1300 (81-3)	Acute Inhalation (rat)	45003202	LC_{50} >5.15 mg/L	IV
870.2400 (81-4)	Primary Eye Irritation (rabbit)	45003203	Not an eye irritant	IV
870.2500 (81-5)	Primary Skin Irritation (rabbit)	45003204	Not a dermal irritant	IV
87.2600 (81-6)	Dermal Sensitization (guinea pig)	45084001	Not a dermal sensitizer	N/A

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile.

Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100	90-Day oral toxicity (rat)	45651504/45651503 (1993/1990); Acceptable/guideline Study I: 0, 50, 100, 200, or 400 ppm (equivalent to 0, 3.52, 6.93, 13.03, and 27.77 mg/kg bw/day, respectively in males and 0, 4.38, 8.64, 17.54, and 34.39 mg/kg bw/day, respectively in females) Study II: 0, 10, 320, or 10,000 ppm (equivalent to 0, 0.7, 22.2, and 713 mg/kg bw/day, respectively in males and 0, 0.8, 24.3, and 754 mg/kg bw/day, respectively in females)	NOAEL = 320 ppm (22.2 mg/kg/day) in males and 50 ppm (4.38 mg/kg/day) in females. LOAEL = 400 ppm (27.77 mg/kg/day) in males based on increased occurrence of extramedullary hematopoiesis and hemosiderosis in spleen; and 100 ppm (8.64 mg/kg/day) in females based on reduction in hemoglobin, hematocrit, and RBC count; increased occurrence of extramedullary hematopoiesis in the spleen and hemosiderosis in the spleen and liver.
870.3200	28-Day dermal toxicity (rat)	45288501 (1998); 0, 75, 400, 1000 mg/kg/day Acceptable/Guideline	Systemic NOAEL = 1000 mg/kg/day. LOAEL = not established. Dermal NOAEL = 1000 mg/kg/day. LOAEL = not established.
870.3700a	Prenatal developmental in (rat)	45082602 (1997); 0, 250, 500, 1000 mg/kg/day Acceptable/Guideline	Maternal NOAEL = 1000 mg/kg/day. LOAEL = not established. Developmental NOAEL = 1000 mg/kg/day. LOAEL = not established.
870.3700b	Prenatal developmental in (rabbit)	45638316, 45638318, 45638317 (1997,1998); 0, 100, 300, 1000 mg/kg/day Acceptable/Guideline	Maternal NOAEL = 1000 mg/kg/day. LOAEL = not established. Developmental NOAEL = 1000 mg/kg/day. LOAEL = not established.

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile.

Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800	Reproduction and fertility effects (rat)	45651505 (Main Study, 1999), 45638319 (Preliminary Study, 1998); 0, 1000, 4000, or 12,000 ppm ; M: 0, 74.2, 297.5, or 894.9 mg/kg/day F: 0, 84.0, 336.7, or 1009.8 mg/kg/day **Acceptable/Guideline**	Parental NOAEL = not established. LOAEL (M/F) = 74.2/84.0 mg/kg/day based on increased absolute and relative spleen weights. Offspring NOAEL = not established. LOAEL (M/F) = 74.2/84.0 mg/kg/day based on increased absolute and relative spleen weights. Reproductive NOAEL (M/F) = 74.2/1009.8 mg/kg/day. LOAEL (M) = 297.5 mg/kg/day based on decreased epididymal sperm counts and increased age of preputial separation in the F_1 generation. Reproductive LOAEL for females was not established.
870.4100a	Chronic toxicity (dog)	45638320 (1999); 0, 10, 100, 1000 mg/kg/day **Acceptable/Guideline**	NOAEL = 10 mg/kg/day. LOAEL = 100 mg/kg/day based on hematologic changes associated with histopathological changes in liver and spleen.
870.4200	Chronic/ Carcinogenicity (rat)	45651506 (1995); 0, 25, 700, or 20,000 ppm test material; M: 0, 1.1, 30.6, and 884.2 mg/kg/day F: 0, 1.4, 39.5, and 1113.5 mg/kg/day **Acceptable/Guideline**	NOAEL (M/F) = 1.1/1.4 mg/kg/day. LOAEL (M/F) = 30.6/39.5 mg/kg/day based on erythrocyte damage and turnover resulting in a regenerative mild anemia. **No Evidence of Carcinogenicity**
870.4300	Chronic/ Carcinogenicity (mouse)	45651507/45877901 (2000/2003); 0, 30, 450, or 7000 ppm test material; M: 0, 3.6, 53.4, or 800.0 mg/kg/day F: 0, 4.3, 63.3, or 913.4 mg/kg/day **Acceptable/Guideline**	NOAEL (M/F) = 3.6/4.3 mg/kg/day. LOAEL (M/F) = 53.4/63.3 mg/kg/day based on increased erythrocyte turnover due to hemoglobin oxidation and resulting in a mild anemia. **No Evidence of Carcinogenicity**
870.5100	Salmonella typhimurium and Escherichia coli Reverse Mutation Assay	44961013 (1997); 0, 312.5, 625, 1250, 2500, or 5000 µg/plate in the presence and absence of metabolic activation (±S9) **Acceptable/Guideline**	Novaluron, tested up to the limit of solubility (2500 µg/plate) and the limit dose (5000 µg/plate), was not cytotoxic with or without S9 activation in four *S. typhimurium* strains and one strain of *E. coli*, and did not induce a genotoxic response in any strain.
870.5100	*Salmonella typhimurium*- bacterial reverse gene mutation assay	45030003 (1986); 0, 10, 33, 100, 333, 1000, or 3333 µg/plate in the presence and absence of mammalian metabolic activation (±S9) **Acceptable/Guideline**	Novaluron, tested up to the limit of solubility (3333 µg/plate), was not cytotoxic with or without S9 activation in five *S. typhimurium* strains, and did not induce a genotoxic response in any strain.
870.5300	Gene Mutation	45638321(1989); 0, 50, 100, 125, 150, 175, or 200 µg/mL with and without metabolic activation (S9-mix) in two independent assays. **Acceptable/Guideline**	There was no evidence of biologically significant induction of mutant colonies over background.

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile.

Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.5375	*In vitro* mammalian chromosome aberration test	44961015 (1992); 40, 200, and 1000 µg/mL, with and without metabolic activation (±S9) Acceptable/Guideline	Novaluron produced no evidence of clastogenic activity in primary human lymphocytes, in the presence or absence of S9 activation.
870.5395	Mammalian erythrocyte micronucleus test in mice	45638322(1989); 0, 1250, 2500, or 5000 mg/kg body weight Acceptable/Guideline	There was no statistically significant increase in the frequency of micronucleated polychromatic erythrocytes in mouse bone marrow at any dose or harvest time.
870.5500	Mutagenicity–Rec assay with *Bacillus subtilis*	44961014 (1998); 50, 150, 500, 1,500, or 5,000 µg/plate, with and without mammalian metabolic activation (±S9) Acceptable/Guideline	Novaluron was equivocal for bacterial DNA damage in the absence of S9 activation, and negative for bacterial DNA damage in the presence of S9 activation.
870.5550	Unscheduled DNA Synthesis in HeLa S3 Human Epithelial cells	45030002 (1988); 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, 128, or 256 µg/mL (±S9) Acceptable/Guideline	Novaluron was considered not to show any evidence of causing DNA damage to HeLa S3 epithelioid cells in this unscheduled DNA synthesis test for mutagenic potential.
870.6200a	Acute neurotoxicity screening battery	45082601 (1999); 0, 200, 650, 2000 mg novaluron/kg Acceptable/Guideline	NOAEL = 650 mg/kg/day. LOAEL = 2000 mg/kg/day based on clinical signs (piloerection, irregular breathing), FOB parameters (increased head swaying, abnormal gait) and neuropathology (sciatic and tibial nerve degeneration).
870.6200b	Subchronic neurotoxicity screening battery	46086204 (2002); 0, 17.5/20.5, 174/207, 1752/2000 mg/kg/day (M/F) Acceptable/Guideline	NOAEL (M/F) = 1752/2000 mg/kg/day. LOAEL = not established.

Table A.2.2. Subchronic, Chronic, and Other Toxicity Profile.

Guideline No.	Study Type	MRID No. (year)/ Classification /Doses	Results
870.7485	Metabolism and pharmacokinetics (rat)	45638401 (2000), 45638323 (1998); single dose of 2 mg/kg or 1000 mg/kg, or 14 multiple 2 mg/kg/day doses of unlabeled novaluron (Lot no. 970211/4, 99.3% chemical purity) followed by a single dose of radiolabeled novaluron. **Acceptable/Guideline**	Novaluron exhibited marginal absorption (16-18%), relatively rapid and complete excretion within 48 hours primarily via the feces and to a lesser extent via urine in rat. Biliary contribution for fecal excretion appears to be insignificant. Absorption appeared to be approaching saturation at high doses. Peak plasma concentration occurred at 2-5 hours. Urinary metabolite profiles revealed 15 components and 8 components following administration of [chlorophenyl-^{14}C]novaluron or [difluorophenyl-^{14}C]novaluron, respectively. The most prevalent urinary metabolite was 2,6-difluorobenzoic acid represented the majority of the urinary radioactivity. Other components individually represented no more than 5.9% of the dose and most represented considerably less than 1%. Parent compound was the most prevalent contributor in the feces. The fecal metabolite profile revealed two metabolites; 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxycthoxy)aniline, and 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea. Quantitatively, these were minor components accounting for <2% of the dose. In the repeated-dose group, some tissues such as fat contained measurable radioactivity at 168 hours post dose but did not appear to suggest significant potential for bioaccumulation or sequestration at the doses tested.
870.7600	Dermal penetration (rat)	45638415 (2000); 1.0, 0.067, 0.0048, or 0.0003 mg/cm^2 **Acceptable/Guideline**	Recovery of administered radioactivity was an acceptable 90.19-105.26%. The maximum total absorbed dose (expressed as percent of administered dose and determined as the sum of radioactivity in excreta, cage wash, untreated skin, fat, blood, and residual carcass) ranged from about 0.5% to 10% of that administered.
870.7600	Immunotoxicity (mouse)	48690105 (2011); 0, 100, 1,000 and 10,000 ppm (0, 21, 200, 2,115 mg/kg/day [F]) **Acceptable/Guideline**	Systemic NOAEL (F) = 2,155 mg/kg/day. Systemic LOAEL was no observed when tested above the limit dose. Immunotoxicity NOAEL (F) = 200 mg/kg/day. Immunotoxicity LOAEL = 2,155 mg/kg/day based on decreased anti-SRBC response.

Appendix B. Physical/Chemical Properties

Table B.1. Physicochemical Properties of Technical Grade Novaluron.		
Parameter	Value	Reference
Melting range	176.5-178.0°C	DP# 315780, 3-NOV-2005, S. Levy
pH	6.5	
Density	1.56 g/cm^3 at 22°C	
Water solubility	3 µg/L at 20°C	
Solvent solubility (at 25°C)	0.00839 g/L in n-heptane 1.88 g/L in xylene 14.5 g/L in methanol 198 g/L in acetone 113 g/L in ethyl acetate 0.98 g/L in n-octanol	
Vapor pressure (mm Hg)	1.2×10^{-7}	
Dissociation constant, pK_a	Not determined due to low water solubility.	
Octanol/water partition coefficient, Log(K_{OW})	4.3 at 25°C	
UV/visible absorption spectrum	Molar absorption coefficients of at 3 maximum absorbances: 15,400 L/mol • cm at 253 nm (neutral) 9,780 L/mol • cm at 253 nm (acidic) 20,500 L/mol • cm at 263 nm (basic)	
Henry's Constant at 25 °C	2×10^{-5} atm•m^3/mol	Product Chemistry, MRID 44961006

Appendix C. Review of Human Research

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from the PHED 1.1, the AHETF database, and the ARTF database are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[7].

[7] http://www.epa.gov/pesticides/science/handler-exposure-data.html and http://www.epa.gov/pesticides/science/post-app-exposure-data.html

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

11/APR/2013

MEMORANDUM: Acute Toxicity Review for CSI Fipronil + Novaluron Spot-On for Dogs

Subject:	Name of Pesticide Product:	CSI Fipronil + Novaluron Spot-On for Dogs
	EPA File Symbol:	53883-GRE
	DP Barcode:	D404002
	Action Code:	R260
	PC Codes:	129121 Fipronil
		124002 Novaluron

From: Tracy Keigwin, Biologist
Technical Review Branch
Registration Division (7505P)

Tracy Keigwin
Brant T. Beard
April 15, 2013

To: Autumn Metzger, RM 07
Insecticide Rodenticide Branch
Registration Division (7505P)

Applicant: Control Solutions, Inc.
5903 Genoa-Red Bluff
Pasadena, TX 77507

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Fipronil	9.8
Novaluron	20.0
Other Ingredient(s):	70.2

Total: 100.0%

ACTION REQUESTED: The Risk Manager requests a review of acute toxicity studies (MRID Nos. 48843204 (870.1100), 48843205 (870.1200), 48843206 (Waiver - 870.1300), 48843207 (870.2400), 48843208 (870.2500) and 48843209 (870.2600) submitted to support the registration of EPA File Symbol 53883-GRE, CSI Fipronil + Novaluron Spot-On for Dogs.

BACKGROUND: Control Solutions, Inc. has submitted an application for EPA File Symbol 53883-GRE, CSI Fipronil + Novaluron Spot-On for Dogs. In support of their application they have submitted MRID Nos 48843204 (870.1100), 48843205 (870.1200), 48843206 (Waiver - 870.1300), 48843207 (870.2400), 48843208 (870.2500) and 48843209 (870.2600). The product label states that CSI Fipronil + Novaluron Spot-On for Dogs kills adult fleas, flea eggs, flea larvae and pupae for up to one month in dogs and puppies meeting the age and weight requirements as stated on the product label. Note that this is a new use (in terms of spot-on treatments) for the active ingredient Novaluron.

GLP: All studies were conducted in accordance with GLP.

DEFICIENCIES/DEVIATIONS: Each of the studies state that the relative humidity was outside the protocol range at times. In addition, the test substance is identified as having a density of 1.0364 g/mL in the acute oral and acute dermal toxicity studies but the certificate of analysis states that the density is 1.056 g/mL. Finally, the purity of the test substance in the primary eye irritation study (MRID 48843207) is not reported, nor does the study contain a certificate of analysis. The test substance name (NF Spot-On) is the same, as is the physical description of the test substance. It is unlikely that any of these deviations affected the acute toxicity profile.

COMMENTS AND RECOMMENDATIONS:

1) The 5 submitted studies (48843204 (870.1100), 48843205 (870.1200), 48843207 (870.2400), 48843208 (870.2500) and 48843209 (870.2600) are acceptable. In addition, TRB accepts the rationale provided in MRID 48843206 and waives the need for an acute inhalation toxicicy study.

2) The product chemistry team must approve the proposed Basic and 4 Alternate CSFs (all dated June 6, 2012) before this action can be finalized.

3) **LABELING:** Based on the toxicity profile above, the following are the precautionary and first aid statements for EPA File Symbol 53883-GRE as obtained from the Label Review System:

PRODUCT ID #: 53883-GRE (53883-312)

PRODUCT NAME: **CSI Fipronil + Novaluron Spot-On for Dogs**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **CAUTION**

Hazards to Humans and Domestic Animals:

Harmful if swallowed. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet.

First Aid:

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Tracy Keigwin **Date:** April 11, 2013
Risk Manager (EPA): 07

The following table is the Acute Toxicity Data Evaluation Record (DER) for the six studies submitted for the proposed product, EPA File Symbol 53883-GRE:

1. DP BARCODE: 404002				
2. PC CODES: 129121 Fipronil and 124002 Novaluron				
3. CURRENT DATE: April 11, 2013				
4. TEST MATERIAL (for acute oral, acute dermal, dermal irritation and dermal sensitization studies): Novaluron/Fipronil Spot-On Product: ECS-F-054 (Lot# ECS-28-109); Amber liquid; 20.43% Novaluron, 10.06% Fipronil; density 1.0364 g/mL; Test substance in eye irritation study: NF Spot-On (Lot: ECS-28-80); clear amber non-viscous liquid.				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Acute oral toxicity / rat Stillmeadow, Inc. (Sugar Land, TX) Study#16185-12/May 22, 2012 OCSPF 870.1100; OECD 425	48843204	LD_{50} Females = 3129 mg/kg bw 1 dosed at 175 mg/kg, 1 at 550 mg/kg, 3 at 1750 mg/kg and 4 at 5000 mg/kg (1 for the initial limit test, 3 for the main test). All survived 175, 550 and 1750 mg/kg. No clinical signs or gross abnormalities were observed in surviving animals. At 5000 mg/kg, all (4/4) died within 1-4 days after test substance administration. Prior to death animals exhibited deceased activity, sensitivity to sound/touch, body tremors, crusted/stained fur, decreased defecation, ocular discharge, piloerection, polyuria, and salivation. At necropsy no gross abnormalities were observed in surviving animals. Gross observations in decedents included stained/matted facial/tail areas, discolored lungs, liver, kidneys and pasty contents of the gastrointestinal tract. The test substance did not affect bodyweight gain in surviving animals.	III	A
Acute dermal toxicity / rat Stillmeadow, Inc. (Sugar Land, TX)	48843205	LD_{50} > 5050 mg/kg bw (both sexes and combined). All survived. Four males (4/5) and four females (4/5)	IV	A

Study#16186-12/May 9, 2012 OCSPP 870.1200; OECD 402		lost or failed to gain weight between study days 0 and 7, however all exceeded their initial weights by study termination Clinical abnormalities observed during the study included decreased activity, decreased defecation, emaciation, piloerection and sensitivity to touch, with all symptoms resolving by study day 5. No signs of dermal irritation were observed. No gross abnormalities observed at necropsy.		
Primary eye irritation / rabbit Stillmeadow, Inc. (Sugar Land, TX) Study#15835-11/December 30, 2011 OCSPP 870.2400; OECD 405	48843207	Minimal irritation. No corneal opacity, iritis or positive signs of conjunctivitis were observed during the study. All (3/3) had a score 1 redness and one had score 1 chemosis at one and 24 hours, resolving within 48 hours, however this is not considered a positive response Maximum average irritation score = 2.7 at the 1 and 24 hour observations.	IV	A
Primary dermal irritation/ rabbit Stillmeadow, Inc. (Sugar Land, TX) Study#16187-12/May 7, 2012 OCSPP 870.2500; OECD 404	48843208	PDII = 1.0 (slightly-irritating). All (3/3) exhibited grade 1 erythema through day 7, resolving within 10 days. One animal (1/3) additionally exhibited grade 1 edema at study day 7 only, resolving within 10 days.	IV	A
Dermal sensitization (Buehler)/Guinea Pig Stillmeadow, Inc. (Sugar Land, TX) Study#16359-12/May 25, 2012 OCSPP 870.2600; OECD 406	48843209	Not a dermal sensitizer. No positive response (grade 1 or higher) was observed in any of the test or naïve control animals at the 24 and 48 hour challenge observation. Grade 1-2 erythema was observed in 10/10 positive control (α-HCA) animals at the 24 hour observation, continuing in 10/10 animals at the 48 hour observation.	Neg	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, D = Data Gap

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

DP Bar Code: 404000; EPA Reg/File No.: 53883-GRE APPLICANT: Control Solutions
DECISION: 465891 PC Code(s): 129121-Fipronil (9.8%) &124002-Novaluron (20.0%)
PRIA: 320-new use for Novaluron

DATE: April 3, 2013

SUBJECT: Product Name: CSI Fipronil + Novaluron Spot On for Dogs.

FROM: Akiva Abramovitch, Ph.D.
Technical Review Branch / RD (7505P)

THROUGH: Shyam Mathur, Ph.D.
Product Chemistry Team Leader
Technical Review Branch/RD (7505P)

4/18/13

TO: Autumn Metzger/John Hebert, PM 7
Insecticide-Rodenticide Branch/ RD (7505C)

Formulation Type: Liquid-Spot on

INTRODUCTION:

The applicant has submitted an application for registration of a new end use product containing Fipronil at 9.8% and Novaluron at 20%. In support of the registration application, the registrant has submitted product chemistry data corresponding to guideline 830 series, group A & group B (MRIDs 488432-01 through 488432-03 and 488432-14 (waiver requests). The CSFs of the basic and alternate formulations 1 through 4 are all dated June 6, 2012 were submitted along with the product label. TRB has been asked to determine the acceptability of the product chemistry data and the proposed CSFs dated 6/6/ 2012.

SUMMARY OF FINDINGS:

1. Name of Active Ingredient: Fipronil (9.8%) and Novaluron (20.0%).

2. Has the registrant claimed substantial similarity to a registered product?

   [ ] Yes; [X] No; [ ] NA; if yes give the registration number of the cited product.

3. All the source materials for the active ingredients are derived from the registered sources:
   [X] Yes; [ ] No.

4. All inert ingredients have been screened by IIAB and found to be approved for the proposed labeled uses: [X] Yes; [ ] No.

5. Confidential Statement of Formula(s):

   [X] Basic and Alternate CSFs 1-4 all dated June 6, 2012;

6. Product label

   a. Ingredient statement: Nominal concentration of AI listed or CSF(s) concur with product label (PR Notice 91-2).

      [X] Yes, if not, explain below:

      Is the sub statement in compliance with PR Notice 97-6 (inert ingredient vs other ingredient)?
      [X] Yes; [ ] No; if not, explain below:

      Metallic equivalent: [ ] Yes [X] NA;
      Soluble arsenic: [ ] Yes [X] NA
      Isomeric ratios: [ ] Yes [X] NA
      Acid equivalent: [ ] Yes [X] NA; {name} acid equiva ent = xx %

   b. Health related sub statements: Product contains?

      Petroleum distillate at > 10%: [ ] Yes [X] No [ ] NA
      Methanol at > 4%: [ ] Yes [X] No [ ] NA
      Sodium nitrate/Sodium nitrite [ ] Yes [X] No [ ] NA

   c. Physical chemical hazard statement: Product label requires a statement per 40 CFR §156.78 for: flammability, explosive potential or electric insulator breakdown?
      [ ] Yes [X] No Flash point of 205F (96 C)

      Is the sub statement in compliance with PR Notice 98-6 (Total Release Fogger)?
      [ ] Yes, [ ] No, [X NA, if not explain below:

   d. Label requires an additional Storage and Disposal statement:
   [ ] Yes [X] No

DP Bar Code: 404000; EPA Reg/File No.: 53883-GRE APPLICANT: Control Solutions
DECISION: 465891 PC Code(s): 129121-Fipronil (9.8%) &124002-Novaluron (20.0%)

7. Group A: Product Chemistry Data

TRB's determination of the acceptability for the proposed product is listed in the tables below.

Guideline No.	Study Title		Data submitted		TRB's Assessment of Data	MRID Nos.
			Yes	No		
830.1550	Product Identity & Composition		X		A	488432-01
830.1600	Description of materials used to produce the product		X		A	488432-01
830.1650	Description of formulation process		X		A	488432-01
830.1670	Discussion on the formation of impurities		X		A	488432-01
830.1700	Preliminary analysis		X		NA	
830.1750	Certified limits (158.350)	Standard certified Limits	X		A	488432-01
		Proposed Limits				
		Justification for wider limits				
830.1800	Enforcement analytical method		X		A (HPLC method for fipronil and novaluron)	488432-02

A = Acceptance, N = Not Acceptable, G = Data Gap, W = Waiver Request, I = In Progress, NA = Not Applicable; U = Upgradeable

8. Group B:

Guideline No.	Study Title	Value or Qualitative Description	TRB's Assessment of Data	MRID Nos.
830.6303	Physical State	Light amber Liquid with botanic odor/scent	A	488432-03
830.6315	Flammability	Not flammable (Flash point above 96 C)	A	488432-03
830.6316	Explodability	NA, not considered to be potentially explosive	A	488432-03
830.7000	pH	Not soluble or dispersable in water	W	488432-14
830.7300	Density (units)	1.0589 specific gravity at 20 C	A	488432-03

A = Acceptance, N = Not Acceptable, G = Data Gap, W = Waiver request,
NA = Not applicable, I = In progress, U = Upgradeable

DP Bar Code: 404000; EPA Reg/File No.: 53883-GRE APPLICANT: Control Solutions
DECISION: 465891 PC Code(s): 129121-Fipronil (9.8%) &124002-Novaluron (20.0%)

CONCLUSIONS:

TRB has reviewed the CSF(s) and product chemistry data for the proposed end use product and has concluded:

1. The proposed CSF for the basic and alternate formulations 1, 2, 3 and 4 all dated June 6, 2012 are acceptable. All the ingredients in the formulations have been approved for the uses cited on the label.

2. The data submitted corresponding to guidelines 830.1550 (product identity and composition), 830.1600 (description of materials used to produce the product) , 830.1650 (description of formulation process), 830.1670 (discussion on the formation of impurity), 830.1750 (certified limits), and 830.1800 (enforcement analytical method) are acceptable.

3. The product chemistry data/waiver requests corresponding to guidelines 830.6302 (color), 830.6303 (physical state), 830.6304 (odor), 830.6314 (oxidation/reduction), 830.6315 (flammability), 830.6316 (explodability), 830.7000 (pH), 830.7100 (viscosity), and 830.7300 (density) are acceptable.

4. The storage stability (guideline 830.6317) and corrosion characteristics (guideline 830.6320) studies were not submitted. These physical/chemical properties are required and it is recommended that observations should be made at 0, 3, 6, 9, and 12 month intervals.

5. The proposed label was screened as it pertains to the product chemistry requirements. The review of the proposed label and uses are the purview of the RM team.

EFFICACY REVIEW

PRODUCT: CSI Fiprinil + Novaluron Spot-on for Dogs

DATE: May 16, 2013

FILE SYMBOL: 53883-GRE

DP BARCODE: 404008

DECISION: 465891

GLP: No

CHEMICALS: Fipronil (9.8%) + Novaluron (20.0%)

CHEMICAL NUMBERS: Fipronil – 129121 Novaluron – 124002

PURPOSE:
New spot-on treatment for dogs. The submitter is citing all data for fipronil, but provided data for the IGR Novaluron for flea eggs/larvae/pupae.

MRIDs:

48843211. Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization.

48843212. Dose Confirmation for a 30 day Claim for a Novaluron Squeeze-On on Dogs Measuring Flea Egg Sterilization.

48843213. Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization.

TEAM REVIEWER: Autumn Metzger

EFFICACY REVIEWER: Autumn Metzger, M.S. 5/16/13

SECONDARY EFFICACY REVIEWER: Jennifer Urbanski, Ph.D. 5/16/13

BACKGROUND

The registrant is seeking to register thisnew product as a topical spot-on insecticide treatment for the control of adult fleas, flea eggs/pupae/larvae, ticks (all life stages), chewing lice, mites and mosquitoes on dogs. All data is being cited for fipronil and data was only provided on flea eggs, pupae and larvae for novaluron.

The proposed dosing of the combination of fipronil + novaluron is as follows:

0-22 lbs = .67ml
23-44 lbs = 1.34 ml
45-88 lbs = 2.68 ml
89-132 lbs = 4.02 ml

DATA REVIEW

The following data review is comprised of explanations of materials and methods, and a summation of experimental results containing tables with reformatted data.

MRID: 48843211. Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization.

Objective

To determine a dosage that would prevent 90% of flea eggs from hatching.

Set Up

There were 7 groups:

Groups B1-B6 = 1 dog each dosed with different potencies of novaluron at levels: 1%, 2.5%, 7.5%, 15%, 30% and 45%

Group 7 = 3 untreated control dogs

Dogs were of random source or purpose bred dogs of varying sex and hair length. Their weights ranged from 22.7 lbs to 27.2 lbs. Ages were not given. Dogs were housed individually in 3x10 ft pens except during flea collections. Dose rates ranged from 0.2-84.1 mg novaluron/ kg of body weight.

Dogs were treated on day 0 and infested with 100 cat fleas on days -1, 1 and then once weekly. After infestations, dogs were kept in cages and flea eggs were collected overnight from the pans below each dog on the 2nd or 3rd day and again on the 6th or 7th day after each infestation.

Eggs were divided into 2 groups of 25. Group 1 eggs were incubated for at least 3 days to measure fertility of the eggs and were recorded as "no. larvae." The other egg group was incubated in a flea growing medium for 35 days and the number of fleas that developed and larvae that hatched were recorded as "no. adults." Percent hatch values were measured for each dog and compared to the control group.

TABLE 1
Dose Titration Probe with Novaluron Squeeze-Ons on Dogs
Measuring Flea Egg Sterilization

Dosage

Dog		Weight		Potency	Dosage	
No.	Group	lb	kg	% w/w	mL	mg/kg *
510	A	23.6	10.7			
357	A	23.5	10.7			
509	A	24.2	11.0			
236	B1	23.6	10.7	45.0%	2.0	84.1
511	B2	27.2	12.3	30.0%	2.0	48.6
233	B3	22.7	10.3	15.0%	2.0	29.1
424	B4	25.1	11.4	7.5%	2.0	13.2
512	B5	23.5	10.7	2.5%	2.0	4.7
234	B6	24.6	11.2	1.0%	1.3	1.2

MS 208D * not adjusted for SG conversion w/w to w/v

TABLE 2
Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Calendar of Events

Day of Study	Treat	Infest	Collect eggs	Count larvae on days
-1		X		
0	Treat			
3			X	6
7			X	10
8		X		
10			X	13
14			X	17
15		X		
17			X	20
21			X	24
22		X		
24			X	27
28			X	31
29		X		
31			X	34
38			X	41

MS 208D

Results

Larvae Emergence-
With the exception of day 21, the 4 higher rates provided ≥90% efficacy and often 100% until day 38. Dose rates of 1.2 and 4.7 mg/kg failed early and were eventually discontinued.

Adult Emergence-
The 4 higher dosages showed 100% efficacy up to day 38.

See tables below.

TABLE 3 (page 1)
Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment [#]			1					3					7							
Dog No.	Group	Dose rate mg/kg		No. Eggs	No. Larvae	% Hatch	Efficacy %	No. Eggs	No. Adults [*]	%	Efficacy %		No. Eggs	No. Larvae	%	Efficacy %		No. Eggs	No. Adults	%	Efficacy %
510	A	Control	I	30	17	57%		33	3	9%			36	23	64%			34	0	0%	
357	A	Control	N	37	12	32%		35	2	6%			37	16	43%			32	2	6%	
509	A	Control	F	34	8	24%		31	2	6%			30	14	47%			31	3	10%	
Mean +/- SD				34	12	38%		33	2	7%			34	18	51%			32	2	5%	
236	B1	84.1	E	38	1	3%	93%	31	0	0%	100%		36	0	0%	100%		40	0	0%	100%
511	B2	48.6		35	1	3%	92%	37	0	0%	100%		31	0	0%	100%		37	0	0%	100%
233	B3	29.1	S	34	0	0%	100%	34	0	0%	100%		32	0	0%	100%		37	0	0%	100%
424	B4	13.2		37	3	8%	78%	34	0	0%	100%		35	0	0%	100%		34	0	0%	100%
512	B5	4.7	T	31	3	10%	74%	35	1	3%	60%		31	5	16%	59%		34	0	0%	100%
234	B6	1.2		34	1	3%	92%	32	1	3%	56%		33	4	12%	76%		38	1	3%	50%

MS 208D

[*] cumulative total of emerged adults & normal pre-emerged pupae
[#] Day after treatment when re-infested and when eggs collected
Table cells left blank, pending adult flea emergence data availability.

TABLE 3 (page 2)
Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment			8	10				14				21				28			
Dog No.	Group	Dose rate mg/kg		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No. Adults	%	Efficacy %	No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No. Adults	%	Efficacy %
510	A	Control	I	33	10	30%		35	1	3%		35	26	74%		35	3	9%	
357	A	Control	N	37	6	16%		37	1	3%		39	10	26%		37	2	5%	
509	A	Control	F	37	3	8%		38	0	0%		39	7	18%		37	3	8%	
				36	6	18%		37	1	2%		38	14	39%		35	3	7%	
236	B1	84.1	E	34	0	0%	100%	34	0	0%	100%	38	0	0%	100%	39	0	0%	100%
511	B2	48.6		35	0	0%	100%	35	0	0%	100%	38	0	0%	100%	36	0	0%	100%
233	B3	29.1	S	39	0	0%	100%	37	0	0%	100%	35	0	0%	100%	39	0	0%	100%
424	B4	13.2		37	0	0%	100%	33	0	0%	100%	35	2	6%	85%	37	0	0%	100%
512	B5	4.7	T	37	4	11%	41%	32	0	0%	100%	37	1	3%	93%	37	0	0%	100%
234	B6	1.2		36	3	8%	54%	32	0	0%	100%	39	2	5%	87%	39	0	0%	100%

MS 208D

* cumulative total of emerged adults & normal pre-emerged pupae

Day after treatment when re-infested and when eggs collected

Table cells left blank, pending adult flea emergence data availability.

TABLE 3 (page 3)

Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility

Egg hatch and adult flea emergence

Day after Treatment			15	17								21							
Dog No.	Group	methoprene mg/kg		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No. Adults	%	Efficacy %	No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No. Adults	%	Efficacy %
510	A	Control	I	39	21	54%		35	4	11%		35	15	43%		38	4	11%	
357	A	Control	N	37	4	11%		40	3	8%		38	10	26%		35	2	6%	
509	A	Control	F	34	13	38%		37	3	8%		38	6	16%		37	3	8%	
				37	13	34%		37	3	9%		37	10	28%		37	3	8%	
236	B1	84.07	E	37	0	0%	100%	38	0	0%	100%	37	0	0%	100%	36	0	0%	100%
511	B2	48.63		35	0	0%	100%	38	0	0%	100%	35	0	0%	100%	37	0	0%	100%
233	B3	28.14	S	38	0	0%	100%	35	0	0%	100%	32	1	3%	89%	35	0	0%	100%
424	B4	13.17		34	0	0%	100%	35	0	0%	100%	38	1	3%	91%	36	0	0%	100%
512	B5	4.69	T	38	11	29%	16%	38	0	0%	100%	35	9	26%	9%	35	0	0%	100%
234	B6	1.17		37	8	22%	37%	39	0	0%	100%	37	13	35%	-24%	37	0	0%	100%

MS 208D

* cumulative total of emerged adults & normal pre-emerged pupae

Day after treatment when re-infested and when eggs collected

Table cells left blank, pending adult flea emergence data availability.

TABLE 3 (page 4)
Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment			22	24								28							
Dog No.	Group	methoprene mg/kg		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No. Adults	%	Efficacy %	No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No Adults	%	Efficacy %
510	A	Control	I	32	16	50%		31	6	19%		34	18	53%		39	6	15%	
357	A	Control	N	38	9	24%		34	3	9%		39	12	31%		37	6	16%	
509	A	Control	F	36	12	33%		32	5	16%		35	7	20%		34	2	6%	
				35	12	36%		32	5	15%		36	12	35%		37	5	12%	
236	B1	84.07	E	37	1	3%	92%	35	0	0%	100%	39	0	0%	100%	38	0	0%	100%
511	B2	48.63		34	0	0%	100%	35	0	0%	100%	35	0	0%	100%	35	0	0%	100%
233	B3	29.14	S	34	1	3%	92%	36	0	0%	100%	36	1	3%	92%	35	0	0%	100%
424	B4	13.17		34	0	0%	100%	36	0	0%	100%	39	1	3%	93%	35	0	0%	100%
512	B5	4.69	T				Discontinued												
234	B6	1.17					Discontinued												

MS 208D

* cumulative total of emerged adults & normal pre-emerged pupae
# Day after treatment when re-infested and when eggs collected
Table cells left blank, pending adult flea emergence data availability.

TABLE 3 (page 5)
Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment				29	31				31				38				38			
Dog No.	Group	methoprene mg/kg		No. Eggs	No. Larvae	%	Efficacy %		No. Eggs	No. Adults	%	Efficacy %	No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	No. Adults	%	Efficacy %
510	A	Control	I	33	10	30%			34	3	9%		20	6	30%		21	2	10%	
357	A	Control	N	38	3	8%			36	1	3%		26	15	58%		20	5	25%	
509	A	Control	F	26	8	31%			36	2	6%		30	10	33%		37	4	11%	
				32	7	23%			35	2	6%		25	10	40%		26		15%	
236	B1	84.07	E	41	0	0%	100%		38	0	0%	100%	36	0	0%	100%	38	0	0%	100%
511	B2	48.63		39	1	3%	89%		37	0	0%	100%	33	0	0%	100%	43	0	0%	100%
233	B3	29.14	S	37	2	5%	78%		37	0	0%	100%	33	0	0%	100%	42	0	0%	100%
424	B4	13.17		35	2	6%	75%		36	0	0%	100%	18	2	11%	72%	15	0	0%	100%
			T																	

MS 208D

* cumulative total of emerged adults & normal pre-emerged pupae
# Day after treatment when re-infested and when eggs collected
Table cells left blank, pending adult flea emergence data availability.

Conclusion

The study established that 13.2 mg/kg (19.6% w/w novaluron) was the minimum dose rate of novaluron for a 1 month flea egg sterilization claim.

Neither marketing claims nor the registration of the product are supported by this study.

48843212. Dose Confirmation for a 30 day Claim for a Novaluron Squeeze-On on Dogs Measuring Flea Egg Sterilization.

Objective
To determine the dosage of novaluron in a spot-on that is efficacious for sterilization of fleas for 30 days.

Set Up

Twelve dogs were divided into one of 2 groups:

Group A (n=6 dogs) = treated w/novaluron at 20% w/w or 13.2 mg/kg
Group B (n= 6 dogs) = untreated controls

Dogs were of random source or purpose bred dogs of varying sex and hair length. Their weights ranged from 15.5 lbs to 35 lbs; ages were not given. Each dog received an exact dosage of 13.2 mg/kg novaluron, which would be the minimum dosage of a 120 lb maximum weight dog. Dogs were housed individually in 3x10 ft runs.

Dogs were treated on day 0 and infested with 100 cat fleas on days 1 (24 hours after treatment) and once weekly afterward until day 35, with the exception of day 21 when fleas were not available. Flea eggs were collected 3 & 7 days after each infestation.

Eggs were sorted into 2 aliquots of ~25 each and incubated for either 3 days to measure the number of eggs that hatched (no. larvae) or incubated in a flea growing medium for 35 days to determine the number of fleas or larvae that developed (no. adults). Day 38 adult emergence tests failed through absence of control emergence. Percent hatch values were calculated for each dog and compared to control group.

TABLE 1
Dose Confirmation with a Novaluron Squeeze-On on Dogs
Measuring Flea Egg Sterilization
Dosage

Group A - controls
Group B - Novaluron Spot-on, Formula # Ecs-F-040, Lot# Ecs-25-65
Potency w/w 20%

Dog		Weight		Dosage	
No.	Group	lb	kg	mL	mg/kg *
510	A	22.4	10.2		
357	A	20.8	9.4		
509	A	23.1	10.5		
454	A	17.5	7.9		
393	A	30.3	13.7		
448	A	34.9	15.8		
Mean		24.8	11.3		
+/- S.D.		6.5	2.9		
422	B	22.4	10.2	0.67	13.2
468	B	35.0	15.9	1.06	13.2
461	B	31.3	14.2	0.94	13.2
498	B	33.9	15.4	1.01	13.2
489	B	18.7	8.5	0.56	13.2
497	B	15.5	7.0	0.46	13.2
Mean		26.1	11.9		
+/- S.D.		8.3	3.8		

MS 203D 2

Results

The mean efficacy for the number of larvae that hatched stayed above 90% up to day 38 and the adult emergence stayed above 90% up to day 35 for treated groups.

The controls for the larvae ranged from 42-72%, which is acceptable. The mean adult emergence in the control group only ranged from 2-29% often with values below 5%, which is unacceptable. The registrant was contacted and asked about rationale for this low control adult emergence and a response was received via email on 2/5/13 from Exponent, the representative of Control Solutions. The response included that these were typical control results from the lab and it is believed that in nature this is compensated by flea's prolific egg production; however there is no data to show the normal adult development ratio in nature. In addition, they felt that it is irrelevant since the egg hatch shows $\geq$ 90% flea egg sterilization for 38 days.

See tables below.

TABLE 3 (page 1)

Dose Confirmation with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility

Egg hatch and adult flea emergence

Day after Treatment #			1				3				7							
Dog No.	Group		No. Eggs	No Larvae	% Hatch	Efficacy %	No. Eggs	* No Adults	%	Efficacy %	No Eggs	No. Larvae	% Hatch	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %
510	A	I	38	31	82%		39	5	13%		40	32	80%		45	16	36%	
357	A	N	35	17	49%		34	4	12%		37	24	65%		40	6	15%	
509	A	F	38	18	47%		40	4	10%		36	11	31%		38	4	11%	
464	A	E	30	21	55%		34	11	32%		40	36	90%		40	18	45%	
393	A	S	38	35	92%		38	13	34%		32	28	88%		43	25	58%	
446	A	T	39	26	67%		40	7	18%		37	29	78%		39	4	10%	
Mean			38	25	65%		38	7	20%		37	27	72%		41	12	29%	
+/- SD			1	7	18%		3	4	11%		3	9	22%		3	9	20%	
422	B	I	40	13	33%	50%	34	0	0%	100%	39	0	0%	100%	41	0	0%	100%
468	B	N	44	0	0%	100%	41	0	0%	100%	40	0	0%	100%	32	0	0%	100%
461	B	F	44	0	0%	100%	36	0	0%	100%	41	0	0%	100%	41	0	0%	100%
498	B	E	40	0	0%	100%	41	0	0%	100%	37	0	0%	100%	38	0	0%	100%
489	B	S	33	0	0%	100%	38	0	0%	100%	39	0	0%	100%	36	0	0%	100%
497	B	T	40	0	0%	100%	40	0	0%	100%	41	0	0%	100%	38	0	0%	100%
Mean			40	2	5%	92%	38	0	0%	100%	40	0	0%	100%	38	0	0%	100%
+/- SD			4	5	13%	20%	3	0	0%	0%	2	0	0%	0%	3	0	0%	0%

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* cumulative total of emerged adults & normal pre-emerged pupae

\# Day after treatment when re-infested and when eggs collected

TABLE 3 (page 2)
Dose Confirmation with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment		7	10								14							
Dog No.	Group		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %	No Eggs	No. Larvae	%	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %
510	A	I	37	25	68%		39	0	0%		38	24	63%		38	0	0%	
357	A	N	32	18	56%		32	0	0%		39	20	51%		37	3	8%	
509	A	F	39	9	23%		36	1	3%		33	14	42%		42	4	10%	
464	A	E	39	23	59%		32	2	6%		34	23	68%		39	6	15%	
393	A	S	36	26	72%		39	2	5%		32	27	84%		38	12	32%	
448	A	T	34	28	82%		30	0	0%		40	29	73%		38	2	5%	
Mean			36	22	60%		35	1	2%		36	23	64%		39	2	12%	
+/- SD			3	7	20%		4	1	3%		3	5	15%			4	11%	
422	B	I	39	0	0%	100%	35	0	0%	100%	37	0	0%	100%	34	0	0%	100%
468	B	N	36	0	0%	100%	38	0	0%	100%	39	0	0%	100%	34	0	0%	100%
461	B	F	36	0	0%	100%	33	0	0%	100%	33	0	0%	100%	35	0	0%	100%
498	B	E	36	0	0%	100%	34	0	0%	100%	32	0	0%	100%	34	0	0%	100%
489	B	S	33	0	0%	100%	34	0	0%	100%	33	0	0%	100%	38	0	0%	100%
497	B	T	34	0	0%	100%	33	0	0%	100%	39	0	0%	100%	39	0	0%	100%
Mean			36	0	0%	100%	35	0	0%	100%	36	0	0%	100%	36	0	0%	100%
+/- SD			2	0	0%	0%	2	0	0%	0%	3	0	0%	0%	2	0	0%	0%

MS 208D 2

* cumulative total of emerged adults & normal pre-emerged pupae
# Day after treatment when re-infested and when eggs collected

TABLE 3 (page 3)
Dose Confirmation with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment			14				17				21							
Dog No	Group		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %	No Eggs	No Larvae	%	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %
510	A	I	36	26	72%		41	2	5%		34	23	68%		38	3	8%	
357	A	N	38	31	82%		37	3	8%		34	21	62%		38	3	8%	
509	A	F	40	21	53%		36	1	3%		39	23	59%		39	2	5%	
464	A	E	42	23	55%		42	6	14%		41	20	49%		37	1	3%	
393	A	S	32	28	88%		36	12	33%		35	28	80%		33	1	3%	
448	A	T	23	18	78%		23	2	9%		31	27	87%		32	3	9%	
Mean			35	25	71%		36	4	12%		36	24	67%		36	2	6%	
+/- SD			7	5	14%		7	4	11%		4	3	14%		3	1	3%	
422	B	I	30	1	3%	95%	33	0	0%	100%	35	0	0%	100%	32	0	0%	100%
468	B	N	38	0	0%	100%	31	0	0%	100%	37	0	0%	100%	35	0	0%	100%
461	B	F	33	0	0%	100%	33	0	0%	100%	19	0	0%	100%	19	0	0%	100%
498	B	E	35	0	0%	100%	37	0	0%	100%	30	0	0%	100%	37	0	0%	100%
489	B	S	35	0	0%	100%	32	0	0%	100%	36	0	0%	100%	19	0	0%	100%
497	B	T	31	0	0%	100%	32	0	0%	100%	33	0	0%	100%	34	0	0%	100%
Mean			34	0	1%	99%	33	0	0%	100%	32	0	0%	100%	29	0	0%	100%
+/- SD			3	0	1%	2%	2	0	0%	0%	7	0	0%	0%	8	0	0%	0%

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* cumulative total of emerged adults & normal pre-emerged pupae

Day after treatment when re-infested and when eggs collected

TABLE 3 (page 4)
Dose Confirmation with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment		14	24								28							
Dog No	Group		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	* No Adults	%	Efficacy %	No Eggs	No Larvae	%	Efficacy %	No Eggs	* No Adults	%	Efficacy %
510	A	I	44	29	66%		39	2	5%		33	23	70%		36	2	6%	
357	A	N	39	19	49%		41	3	7%		34	26	76%		36	2	5%	
509	A	F	41	14	34%		45	3	7%		37	11	30%		35	1	3%	
464	A	E	39	26	67%		43	5	12%		37	27	73%		37	1	3%	
393	A	S	35	31	89%		37	4	11%		34	24	71%		33	1	3%	
448	A	T	29	19	66%		32	1	3%		34	13	38%		33	2	6%	
Mean			38	23	62%		40	3	7%		35	21	60%		36	2	4%	
+/- SD			5	7	18%		5	1	3%		2	7	20%		2	1	2%	
422	B	I	30	0	0%	100%	31	0	0%	100%	24	4	17%	72%	6	0	0%	100%
466	B	N	40	0	0%	100%	39	0	0%	100%	38	1	3%	96%	35	0	0%	100%
461	B	F	16	0	0%	100%	16	0	0%	100%	20	0	0%	100%	22	0	0%	100%
498	B	E	38	1	3%	96%	40	0	0%	100%	38	1	3%	96%	37	0	0%	100%
489	B	S	24	2	8%	86%	24	0	0%	100%	8	0	0%	100%	8	0	0%	100%
497	B	T	32	0	0%	100%	33	0	0%	100%	19	1	5%	91%	10	0	0%	100%
Mean			30	1	2%	97%	31	0	0%	100%	25	1	5%	92%	20	0	0%	100%
+/- SD			9	1	3%	5%	9	0	0%	0%	12	1	6%	11%	14	0	0%	0%

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* cumulative total of emerged adults & normal pre-emerged pupae

[a] Day after treatment when re-infested and when eggs collected

TABLE 3 (page 5)
Dose Confirmation with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization

Post-treatment Flea Egg Fertility
Egg hatch and adult flea emergence

Day after Treatment		28	31								35							
Dog No.	Group		No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %	No. Eggs	No. Larvae	%	Efficacy %	No. Eggs	* No. Adults	%	Efficacy %
510	A	I	32	6	19%		35	1	3%		33	13	39%		33	2	6%	
357	A	N	35	16	46%		39	2	5%		32	24	75%		35	2	6%	
509	A	F	39	10	26%		37	1	3%		37	14	38%		38	0	0%	
464	A	E	36	9	25%		38	0	0%		37	14	38%		39	0	0%	
393	A	S	31	18	58%		38	3	8%		34	27	79%		34	2	6%	
448	A	T	38	31	82%		36	3	8%		32	29	91%		33	3	9%	
Mean			35	15	42%		38	2	4%		34	20	60%		35	2	4%	
+/- SD			3	9	24%		1	1	3%		2	7	24%		3	1	4%	
422	B	I	39	0	0%	100%	37	0	0%	100%	34	2	6%	90%	37	0	0%	100%
466	B	N	38	0	0%	100%	34	0	0%	100%	38	3	8%	87%	36	0	0%	100%
461	B	F	35	1	3%	93%	37	0	0%	100%	38	0	0%	100%	38	0	0%	100%
498	B	E	32	0	0%	100%	38	0	0%	100%	32	0	0%	100%	34	0	0%	100%
469	B	S	35	0	0%	100%	32	0	0%	100%	30	2	7%	89%	30	0	0%	100%
497	B	T	39	1	3%	94%	33	0	0%	100%	38	0	0%	100%	35	0	0%	100%
Mean			36	0	1%	98%	36	0	0%		35	1	3%	94%	35	0	0%	100%
+/- SD			3	1	1%	3%	2	0	0%		4	1	4%	6%	3	0	0%	0%

MS 208D 2

* cumulative total of emerged adults & normal pre-emerged pupae
# Day after treatment when re-infested and when eggs collected

Conclusion
The data show that the product kills flea eggs; however based on the poor control performance, data do not prove that it kills flea larvae or pupae or "all life stages" of fleas.

48843213. Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (Ctenocephalides felis) and Ticks (Rhipicephalus sanguineus) on Dogs.

Objective
To compare the labeled dose of the novaluron spot-on to an untreated control and Merial's Frontline Plus for dogs in controlling adult cat fleas and Brown dog ticks.

Set Up

Eighteen dogs were divided in to 3 groups:

Group A (n=6 dogs) = untreated controls
Group B (n= 6 dogs) = treated with fipronil – 9.8%, novaluron at 20% (as labeled .67ml for dogs <22 lbs and 1.34 ml for dogs >22 lbs)
Group C (n=6) =Frontline Plus for dogs, fipronil + S-Methoprene (EPA Reg No. 65331-5)

Dogs were treated on day 0 and infested with 100 cat fleas and 50 *R. sanguineus* ticks on days -1, 7, 14, 21, & 28. Flea/tick counts were performed ~24 hours after infestation and again 48 hours later and were removed at 48 hours.

Efficacy was determined by the mean number of live fleas/ticks on the treated vs. untreated controls.

Results

Flea
Novaluron treated dogs had >90% efficacy at every 24 hour and 48 hour count (typically at 100%) up to day 30 (see tables below).

Tick
Novaluron treated dogs had >90% efficacy at every 48 hour count up to day 30 and every 24 hour count up to day 30 with the exception of day 1 which had 76% efficacy (see tables below).

TABLE 3 (Page 1)
Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (Ctenocephalides felis) and Ticks (Rhipicephalus sanguineus) on Dogs.
Flea Counts

Days after Treatment		0	1		2		8		9		15		16	
Dog no.	Group		No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %
431	A		29		27		35		33		61		77	
506	A		27		30		31		32		62		60	
236	A		36		35		42		40		68		62	
411	A		22		24		45		40		57		51	
234	A		26		25		39		35		52		47	
378	A		28		26		33		38		49		48	
Mean			28.0		27.8		37.5		35.0		51.5		57.5	
+/- S.D.			4.6		4.1		5.4		4.2		11.7		11.4	
482	B		1	96%	0	100%	0	100%	0	100%	0	100%	0	100%
222	B		0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
520	B		0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
482	B		0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
483	B		0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
448	B		0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
Mean			0.2	99%	0.0	100%	0	100%	0	100%	0.0	100%	0.0	100%
+/- S.D.			0.4	1%	0.0	0%	0.0	0%	0.0	0%	0.0	0%	0.0	0%
229	C		0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
301	C		12	57%	0	100%	0	100%	0	100%	0	100%	0	100%
357	C		9	68%	0	100%	0	100%	0	100%	0	100%	0	100%
424	C		10	64%	0	100%	0	100%	0	100%	0	100%	0	100%
380	C		6	79%	0	100%	0	100%	0	100%	0	100%	0	100%
515	C		4	86%	0	100%	0	100%	0	100%	0	100%	0	100%
Mean			6.8	76%	0.0	100%	0	100%	0	100%	0.0	100%	0.0	100%
+/- S.D.			4.4	16%	0.0	0%	0.0	0%	0.0	0%	0.0	0%	0.0	0%

MS 222D — Infestations were with 100 fleas

Flea Tables

TABLE 3 (Page 2)

Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (Ctenocephalides felis) and Ticks (Rhipicephalus sanguineus) on Dogs.

Flea Counts

Days after Treatment		21	22		23		28	29		30	
Dog no.	Group		No.	Eff %	No.	Eff %		No.	Eff %	No.	Eff %
431	A	Day	47		40		Day	39		40	
506	A	Day	45		43		Day	48		47	
236	A	Day	70		68		Day	57		55	
411	A	Day	54		52		Day	60		60	
234	A	Day	50		48		Day	50		53	
378	A	Day	39		36		Day	38		37	
Mean			49.8		47.8			48.7		48.7	
+/- S.D.			11.3		11.4			9.0		8.0	
0											
482	B	Day	0	100%	0	100%	Day	0	100%	0	100%
222	B	Day	0	100%	0	100%	Day	0	100%	0	100%
520	B	Day	0	100%	0	100%	Day	0	100%	0	100%
462	B	Day	0	100%	0	100%	Day	0	100%	0	100%
483	B	Day	0	100%	0	100%	Day	0	100%	0	100%
448	B	Day	0	100%	0	100%	Day	0	100%	0	100%
Mean			0.0	100%	0.0	100%		0	100%	0	100%
+/- S.D.			0.0	100%	0.0	0%		0.0	0%	0.0	0%
0											
229	C	Day	0	100%	0	100%	Day	0	100%	0	100%
301	C	Day	0	100%	0	100%	Day	0	100%	0	100%
357	C	Day	0	100%	0	100%	Day	0	100%	0	100%
424	C	Day	0	100%	0	100%	Day	0	100%	0	100%
380	C	Day	0	100%	0	100%	Day	0	100%	0	100%
515	C	Day	0	100%	0	100%	Day	0	100%	0	100%
Mean			0.0	100%	0.0	100%		0	100%	0	100%
+/- S.D.			0.0	0%	0.0	0%		0.0	0%	0.0	0%

MS 222D

Infestations were with 100 fleas

TABLE 4 (page 1)

Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (Ctenocephalides felis) and Ticks (Rhipicephalus sanguineus) on Dogs.

Tick Counts

Days after Treatment		0	1		2		8		9		15		16	
Dog no.	Group		No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %
431	A		12		13		22		20		45		43	
506	A		19		18		19		17		39		35	
236	A		17		15		17		16		43		38	
411	A		11		13		27		25		35		31	
234	A		11		10		18		16		40		39	
378	A		20		18		20		18		32		31	
Mean			15.0		14.5		20.5		18.7		39.2		36.2	
+/- S.D			4.1		3.1		3.6		3.4		4.7		4.8	
0														
482	B		4	73%	2	86%	0	100%	0	100%	0	100%	0	100%
222	B		6	60%	3	79%	0	100%	0	100%	0	100%	0	100%
520	B		4	73%	0	100%	0	100%	0	100%	6	85%	1	97%
462	B		3	86%	0	100%	0	100%	0	100%	0	100%	0	100%
483	B		2	87%	0	100%	0	100%	0	100%	0	100%	0	100%
448	B		3	80%	0	100%	0	100%	0	100%	0	100%	0	100%
Mean			3.7	76%	0.8	94%	0	100%	0	100%	1.0	97%	0.2	100%
+/- S.D.			1.4	9%	1.3	9%	0.0	0%	0.0	0%	2.4	5%	0.4	1%
0														
229	C		11	27%	2	86%	0	100%	0	100%	0	100%	0	100%
301	C		9	40%	6	59%	0	100%	0	100%	0	100%	0	100%
357	C		8	47%	3	79%	0	100%	0	100%	0	100%	0	100%
424	C		9	40%	4	72%	0	100%	0	100%	0	100%	0	100%
380	C		3	80%	3	79%	0	100%	0	100%	0	100%	0	100%
515	C		1	93%	5	66%	0	100%	0	100%	0	100%	0	100%
Mean			6.8	54%	3.0	74%	0	100%	0	100%	0.0	100%	0.0	100%
+/- S.D.			3.9	26%	1.5	10%	0.0	0%	0.0	0%	0.0	0%	0.0	0%

MS 2220

Infestations were with 50 *R. sanguineus* ticks

TABLE 4 (page 2)

Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (Ctenocephalides felis) and Ticks (Rhipicephalus sanguineus) on Dogs.

Tick Counts

Days after Treatment		21		22		23		28		29		30	
Dog no.	Group	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %	No.	Eff %
431	A	39		37		41		39					
506	A	45		44		48		48					
236	A	46		42		40		57					
411	A	43		43		45		60					
234	A	42		40		39		50					
378	A	37		38		37		36					
Mean		42		40.7		41.3		48.7					
+/- S.D.		3.5		2.8		3.5		3.0					
0													
482	B	0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
222	B	0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
520	B	1	98%	0	100%	4	90%	0	100%	0	100%	0	100%
462	B	0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
483	B	0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
448	B	0	100%	0	100%	0	100%	0	100%	0	100%	0	100%
Mean		0.2	100%	0.0	100%	0	100%	0	100%	0	100%	0	100%
+/- S.D.		0.4	0%	0.0	0%	1.6	4%	0.0	0%				
0													
229	C	0	100%	0	100%	1	98%	0	100%				
301	C	0	100%	0	100%	1	98%	0	100%				
357	C	0	100%	0	100%	0	100%	0	100%				
424	C	0	100%	0	100%	0	100%	0	100%				
380	C	0	100%	0	100%	0	100%	0	100%				
515	C	0	100%	0	100%	0	100%	0	100%				
Mean		0.0	100%	0.0	100%	0.5	99%	0	100%				
+/- S.D		0.0	0%	0.0	0%	1%		0.0	0%				

MS 2220 Infestations were with 50 *R. sanguineus* ticks

Conclusion

The dose given of the fipronil + novaluron combination product was efficacious against adult cat fleas and adult *R. sanguineus* ticks on dogs for up to 30 days.

Claims

The following claims are **acceptable**:

- Any claim referring to killing adult fleas or flea eggs for up to 1 month [30 days]
- All claims on proposed label for ticks, mosquitoes and chewing lice are acceptable based on cited data provided

The following claims are **not acceptable** based on the data provided and must be removed from the proposed label:

- Any claim referring to flea larvae or pupae
- Any claim referring to "All life stages" of fleas
- "Completely" breaks the flea life cycle
- "Seven and 8 way protection" needs to be revised to not include flea larvae and pupae

Other claims:

- Revise the weights for dogs as according to the companion animal safety memo
- Qualify "long lasting"
- Delete "specially formulated"

In addition, delete the following claims as they were not tested on this combination:

- "Fast acting"
- "Dogs can be bathed 24 hours after treatment"
- "Patented technology"
- "Waterproof"
- "Remains effective even after bathing, water immersion, or exposure to sunlight"

RE: 53883-GRE, efficacy question
James Messina to: Autumn Metzger 02/05/2013 09:04 AM
Cc: "Anne Turnbough (aturnbough@ControlSolutionsInc.com)"

History: This message has been forwarded.

Dear Autumn,

We reviewed EPA's question regarding the efficacy data (MRID 488432212) submitted to support the pending registration application under 53883-GRE. The Agency noted that this study demonstrated low adult emergence for the controls (often below 6%) on many of the days. We contacted the performing laboratory and the study author (Tom Miller, Ph.D.) and Dr. Miller provided the following response:

The procedures that are used in the adult flea emergence component of these studies have historically not resulted in high control adult flea emergence ratios at 1 month after incubation, because this system is artificial. In nature, this low yield of adults is compensated by the high biotic potential of the flea's prolific egg production. In most biological systems, that do not have parental care, juvenile survival to adulthood of 5% is a high estimate and in many systems it is much less than 1%. There are no data to actually show what is the normal adult development ratio from flea eggs in nature, i.e., the dog's home environment.

The concern about adult flea emergence is for practical purposes irrelevant since the egg hatch data shows 90% and higher flea egg sterilization for 38 days, 8-10 days beyond the proposed 1 month label claim. No flea egg survival means no adult flea emergence. Irrespective of the low control emergence results, these values are close to, or better than the flea egg hatch inhibition data for the same date. Also higher efficacy based on adult flea emergence is to be anticipated, since the developing flea larvae in the culture media preferentially feed off adult flea frass (that's why their guts are usually colored red) and the frass is usually contaminated with the IDI, as are the egg shells from which these larvae hatch. Because the eggs picked out the amount of essential frass is miniscule, compared with nature.

We hope that the above addresses the Agency's question. If you need additional information, please contact Anne or me.

Best Regards,

James Messina
Exponent
202.772.4932 office
301.908.1181 mobile

From: Metzger.Autumn@epamail.epa.gov [mailto:Metzger.Autumn@epamail.epa.gov]
Sent: Tuesday, January 15, 2013 11:41 AM
To: James Messina
Subject: 53883-GRE, efficacy question

Hello James,

In reviewing the efficacy data for the IGR qualities of Novaluron, MRID 48843212 has very low adult emergence for the controls often below 6% on many of the days. I am not seeing anything in the report to discuss why this may have occurred or why the data should be considered acceptable. We will need some sort of rationale in writing.

Autumn Metzger
Biologist
U.S. Environmental Protection Agency
Insecticide-Rodenticide Branch
Registration Division (7505P)
1200 Pennsylvania Ave. NW
Washington, DC 20460

Tel: 703 305-5314
Fax: 703 308-5433
Email: metzger.autumn@epa.gov

CSI Revised End-Use Formulation

James Messina to: John Hebert 11/16/2012 12:58 PM

Cc: Autumn Metzger, "Anne Turnbough (aturnbough@ControlSolutionsInc.com)" , Matthew Feinberg

John,

On behalf of our client Control Solutions, Inc. (CSI), Exponent is requesting to withdraw our October 18, 2012 submission (attached) of a new end-use formulation for EPA File Symbol 53883-GRE. We request that the data (with assigned MRIDs) be left on file with EPA as we plan to cite it in a future submission.

If you have any questions, please contact me.

keeping original formulation + PRIA date though in play!

Best Regards,

James Messina
Principal Regulatory Consultant
Exponent
Center for Chemical Regulation and Food Safety
1150 Connecticut Avenue, N.W.
Suite 1100
Washington, DC 20036
202-772-4932
202-772-4979 fax
301-908-1181 cell

Fip+Novaluron Cover Letter 10-18-2012.pdf.pdf

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

November 06, 2012

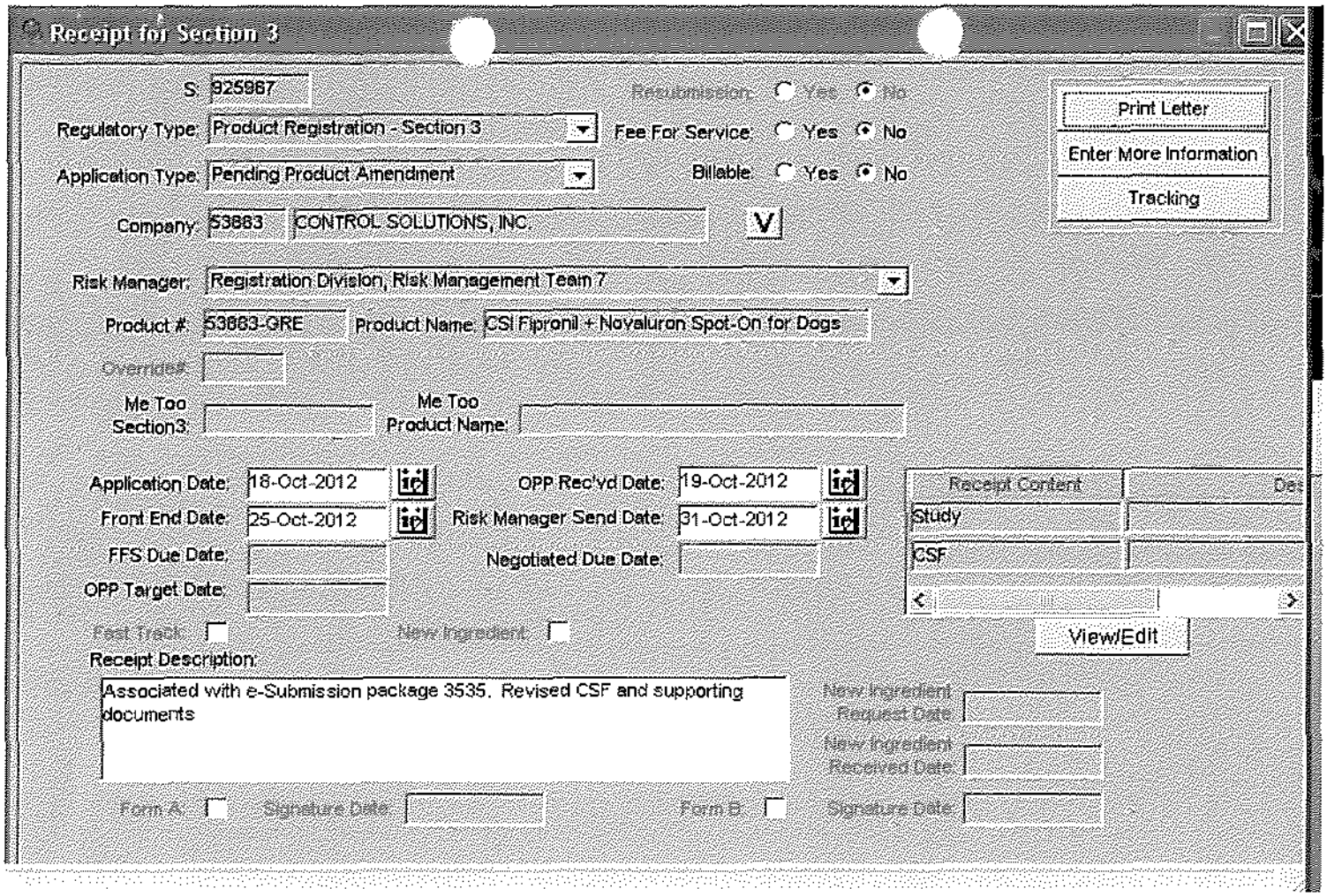
OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

CONTROL SOLUTIONS, INC.
5903 GENOA-RED BLUFF ROAD
PASADENA, TX 77507-1041

Report of Analysis for Compliance with PR Notice 11-03

Thank you for your submittal of 19-OCT-12. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 11-03. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.



Resubmission

- Autumn - see my ~~your~~ email about this one. Once they respond we can talk about renegotiating - What do you think about the solvent change?

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

October 31, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

ANNE TURNBOUGH, PH.D.
CONTROL SOLUTIONS, INC.
5903 GENOA-RED BLUFF ROAD
PASADENA, TX 77507-1041

PRODUCT NAME: CSI Fipronil + Novaluron Spot-On for Dogs
COMPANY NAME: CONTROL SOLUTIONS, INC.
OPP IDENTIFICATION NUMBER:
EPA FILE SYMBOL: 53883-GRE
EPA RECEIPT DATE: 10/19/12

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 7, at (703) 308-6249.

Sincerely,

Front End Processing Staff
Information Services Branch
Information Technology & Resources Management Division

Fee for Service

{925967\~

This package includes the following

- ○ New Registration
- ◉ Amendment

□ Studies? □ Fee Waiver?

□ volpay % Reduction: ____

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 7

Receipt No. S- 925967

EPA File Symbol/Reg. No. 53883-GRE

Pin-Punch Date: 10/19/2012

□ This item is NOT subject to FFS action.

Action Code:

Requested:

Granted:

Amount Due: $ _____

Parent/Child Decisions:

☒ Inert Cleared for Intended Use ☒ Uncleared Inert in Product

Reviewer: _____ Date: 10/31/12

Remarks:

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States Environmental Protection Agency Washington, DC 20460

☒ Registration ☐ Amendment ☐ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
53883-GRE	John Hebert	☒ None ☐ Restricted
4. Company/Product (Name) Control Solutions, Inc./CSI Fipronil + Novaluron Spot-on for Dogs	5.PM# 7	

5. Name and Address of Applicant *(Include ZIP Code)*
Control Solutions, Inc.
5903 Genoa Red Bluff
Pasadena, TX 77507

☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of additional support data for a registration application for the new end-use product CSI Fipronil + Novaluron Spot-on for Dogs.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☒ Yes* ☐ No	☒ Yes ☐ No	☐ Yes ☒ No	☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag
***Certification must be submitted**	If "Yes" Unit Packaging wgt. 0.023 fl oz (0.67 ml) 0.045 fl oz (1.34 ml) 0.091 fl oz (2.68 ml) 0.136 fl oz (4.02 ml) — No. per Container 1, 2, 3, 4, 5, 6, 12, 24 vials	If "Yes" Package wgt. — No. per Container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	0.023 fl oz (0.67 ml), 0.045fl oz (1.34 ml), 0.091 fl oz (2.68 ml), 0.136 fl oz (4.02 ml)	☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☒ Other _____ ☐ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Anne Turnbough	Director, Regulatory Affairs	281-892-2532

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature	3. Title
BY: Anne M Turnbough	Director, Regulatory Affairs
4. Typed Name: Anne Turnbough	5. Date: 10/18/2012

Pages 132-134 - Claimed confidential by submitter

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:

Control Solutions, Inc. (EPA Company No.53883)
5903 Genoa Red Bluff
Pasadena, TX 77507-1041

CONTACT PERSON (Return to)

Anne Turnbough
Control Solutions, Inc.
5903 Genoa Red Bluff
Pasadena, TX 77507-1041

REGULATORY ACTION SUPPORTED BY THIS PACKAGE:

This submission is to provide additional support information for the pending the EPA registration application for the new end-use product CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-GRE).

SUBMITTAL DATE:

October 18, 2012

Volume	Study Title	MRID No.
1	Administrative Materials	48932300
2	Group A Product Chemistry for the End-Use Product CSI Fipronil + Novaluron Spot-On for Dogs	48932301
3	NF2 Spot-On Product Chemistry	48932302
4	NF2 Spot-On Acute Oral Toxicity (UDP) in Rats	48932303
5	NF2 Spot-On Acute Dermal Toxicity in Rats	48932304
6	NF2 Spot-On Acute Inhalation Toxicity in Rats	48932305
7	Acute Eye Irritation Study in Rabbits	48932306
8	NF2 Spot-On Acute Dermal Irritation in Rabbits	48932307
9	NF2 Spot-On Skin Sensitization in Guinea Pigs	48932308

CONTROL SOLUTIONS incorporated
A Mukhteshim-Agan Company

October 18, 2012

John Hebert, PM7
Office of Pesticide Programs (7504P) (REGFEE)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: Pending Registration Application Support for a Revised End-Use Formulation
CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-GRE)

Dear Mr. Hebert:

Please find enclosed a CD that contains a revised application package for the pending Pesticide Registration Application for CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-GRE). Included on this CD is:

- Transmittal Document;
- Application for Pesticide Registration (EPA Form 8570-1);
- Revised Confidential Statement of Formula (Basic and Alternates, EPA Form 8570-4);
- Formulator's Exemption Statement (EPA Form 8570-27);
- Certification with Respect to Citation of Data (EPA Form 8570-34);
- Revised Data Matrix (EPA Form 8570-35) - EPA and Public Versions; and
- Copies of the Supporting Studies.

Should you have any questions regarding this CD, or any of the files contained within, please do not hesitate to contact me at aturnbough@controlsolutionsinc.com or at 281-892-2532.

Sincerely,

Anne M. Turnbough

Anne Turnbough Ph.D.
Director, Regulatory Affairs

Enclosures

Form approved. OMB No. 2070-0060, 2070-0057, 2070-0107, 2070-0122, 2070-0164.

EPA

United States
Environmental Protection Agency
Washington, DC 20460

Formulator's Exemption Statement

(40 CFR 152.85)

Applicant's Name and Address	EPA File Symbol/Registration Number
Control Solutions, Inc. 5903 Genoa Red Bluff Pasadena, TX 77507-1041	53883-NEW
	Product Name CSI Fipronil + Novaluron Spot-On for Dogs
	Date of Confidential Statement of Formula *(EPA Form 8570-4)* 09/25/2012

As an authorized representative of the applicant for registration of the product identified above, I certify that:

(1) This product contains the following active ingredient(s):

Fipronil
Novaluron

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging another product which contains that active ingredient which is registered under FIFRA Section 3, is purchased by us from another person and meets the requirements of 40 CFR section 158.50(e)(2) or (3).

(3) Indicate by checking (A) or (B) below which paragraph applies:

☑ (A) An accurate Confidential Statement of Formula *(EPA FORM 8570-4)* for the above identified product is attached to this statement. That formula statement indicates, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1).

OR

☐ (B) The Confidential Statement of Formula (CSF)(EPA Form 8570-4) referenced above and on file with the EPA is complete, current, an accurate and contains the information required on the current CSF.

(4) The following active ingredients in this product qualify for the formulator's exemption.

Source

Active Ingredient	Product Name	Registration Number
Fipronil [redacted]	[redacted]	[redacted]
Fipronil [redacted]	[redacted]	[redacted]
Fipronil [redacted]	[redacted]	[redacted]
Fipronil [redacted]	[redacted]	[redacted]
Novaluron [redacted]	[redacted]	[redacted]

Signature	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	10/18/2012

EPA Form 8570-27 (Rev. 06-2004)

Copy 1 – EPA
Copy 2 - Applicant copy

Product ingredient source information may be entitled to confidential treatment

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Control Solutions, Inc., 5903 Genoa Red Bluff Pasadena, TX 77507	EPA Registration Number/File Symbol 53883-GRE
Active Ingredient(s) and/or representative test compound(s) Fipronil and Novaluron	Date October 18, 2012
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor non-food	Product Name CSI Fipronil + Novaluron Spot-On for Dogs

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).	☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (I) to pay compensation to the extent required by sections 3(c)(1)(F) andfor 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Anne M Turnbough	10/18/2012	Anne Turnbough, Director, Regulatory Affairs

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version.

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: October 18, 2012	EPA Reg No./File Symbol 53883-GRE	Page 1 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fiprnnil + Novaluron Spot-on for Dogs	
Ingredients: Fipronil, Novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1700, 830.1750	Group A Product Chemistry	48843201 48932301	Control Solutinns, Inc.	OWN	
830.1800	Enforcement analytical method	48843202	Control Solutions, Inc.	OWN	
830.6302, 830.6303, 830.6304, 830.6313, 830.6315, 830.7100, 830.7300	Group B Product Properties	48843203 48932302	Control Solutions, Inc.	OWN	
830.6314, 830.6316, 830.6317, 830.6319, 830.6320, 830.6321, 830.7520	Waiver Request for Group B Product Properties	48843214	Control Solutions, Inc.	OWN	
830.6317, 830.6320	Storage stability and corrosion characteristics	To be conducted	Control Solutions, Inc.	OWN	
870.1100	Acute oral toxicity	48843204 48932303	Control Solutions, Inc.	OWN	
870.1200	Acute dermal toxicity	48843205 48932304	Control Solutions, Inc.	OWN	
870.1300	Acute inhalation toxicity	48843206 48932305	Control Solutions, Inc.	OWN	
870.2400	Primary eye irritation	48843207 48932306	Control Solutinns, Inc.	OWN	
870.2500	Primary dermal irritation	48843208 48932307	Control Solutions, Inc.	OWN	
870.2600	Dermal sensitization	48843209 48932308	Control Solutions, Inc.	OWN	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.67 mL Capacity	48703501	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 1.34 mL Capacity	48703502	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 2.68 mL Capacity	48652701	Horizon Valley Generics, Inc.	PER	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 4.02 mL Capacity	48703503	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	

Signature: Anne M Turnbough	Name and Title Anne Turnbough, Director, Regulatory Affairs	Date 10/18/2012

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DATA MATRIX

Date: October 18, 2012	EPA Reg No./File Symbol 53883-NEW	Page 2 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	

Ingredients: Fipronil, Novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
NA	Child Resistant Packaging Study Test Summary Report: Thermoforme Blister Pack for Pipettes of 0.5 mL Capacity, 0.67 mL Capacity, 1.34 mL Capacity, 2.68 mL Capacity, 4.02 mL Capacity	48703504	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	
NA	Use of One Tube 1x Child Resistaot Unit Packaging Data (Child and Senior) to Support All Unit Configurations for Fipronil Based Spot-On Registrations	48614201	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze On 0.67ml White Applicator with Orange Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48614202	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze On 1.34ml White Applicator with Green Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48614203	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 2.68ml White Applicator with Red Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Product, Inc.	48614204	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze On 4.02ml White Applicator with Blue Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48614205	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 0.67ml White Applicator with Orange Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48059803	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 1.34ml White Applicator with Green Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	4859804	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 2.68ml White Applicator with Red Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products. Inc.	4859805	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 4.02ml White Applicator with Blue Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	4859806	Sergeant's Pet Care Products, Inc.	PER	

Signature: Anne M Turnbough	Name and Title Anne Turnbough, Director, Regulatory Affairs	Date 10/18/2012

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DATA MATRIX

Date: October 18, 2012	EPA Reg No./File Symbol 53883-NEW	Page 3 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	

Ingredients: Fipronil, Novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
40 CFR 157	Evaluation of the Cat Squeeze On 0.5 ml White Applicator with Purple Label Indicator (3x), scissors to open – Fail as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48650101	Sergeant's Pet Care Products, Inc.	PER	
870.7200	General Safety Evaluation of fipronil-Novaluron Spot-on in 8-Week-Old Puppies and Adult Dogs	48843210	Control Solutions, Inc.	OWN	
870.7200	Arnaud, J.; Consalvi, P. (1993) Assessment of Tolerance of a 0.25% RM 1601 Spray Formulation in Dogs at 3, 9, and 15 ml/kg When Applied 6 times in the Haircoat at 28 Day Intervals: Revised: Lab Project Number CLI138. Unpublished study prepared by Rhone Merieux, Inc. 69 p.	43121110	MERIAL LIMITED	OLD	
870.7200	Arnaud, J.; Consalvi, P. (1993) Domestic Animal Safety: Assessment of the Tolerance of a 0.25% RM 1601 Spray in Nursing Puppies Administered Twice at a 28 Day Interval at a Dose Rate of 6 ml/kg: Revised: Lab Project Number CLI 180. Unpublished study prepared by Rhone Merieux, Inc. 32 p.	43121111	MERIAL LIMITED	OLD	
870.7200	Schwartz, E. (1994) Domestic Animal Safety Study of RM1601C Topical Spray (Frontline Spray Treatment) in Juvenile Dogs: Lab Project Number: 94423: PS-232DAS. Unpublished study prepared by White Eagle Toxicology Labs. 171 p.	43444905	MERIAL LIMITED	OLD	
870.7200	Walker, K. (1995) Discussion in Support of Bridging Domestic Animal Safety Data on Frontline Spray Treatment to Frontline Spot Treatment Data Package. Unpublished study prepared by Rhone Merieux, Inc. 6 p.	43577711	MERIAL LIMITED	OLD	
870.7200	Powell, L.; Paffett, R. (1995) Domestic Animal Safety Study by Topical Administration to Dogs: Fipronil Spot Treatment (RM 1601E): Lab Project Number: MRX 23/950406. Unpublished study prepared by Huntingdon Research Centre, Ltd. 219 p.	43863802	MERIAL LIMITED	OLD	
810.3300	Everett, R.; Cunningham, J. (1993) A Dose Titration Study to Determine the Optimal Spray Concentration of RM 1601 for Long Term Control of the Cat Flea Ctenocephalides felis and the Brown Dog Tick Rhipicephalus sanguineus in the Dog: Revised: Lab Project Number: RMD 292: P/214LT. Unpublished study prepared by Agrescarch Consultants. 53 p.	43121114	MERIAL LIMITED	OLD	

Signature: Anne M Turnbough	Name and Title Anne Turnbough, Director, Regulatory Affairs	Date 10/18/2012

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Date: October 18, 2012	EPA Reg No./File Symbol 53883-NEW	Page 4 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	
Ingredients: Fipronil, Novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Cruthers, L. (1993) Product Performance: A Dose Confirmation Study to Verify the Optimal Spray Concentration of RM 1601 for Long Residual Control of the Cat Flea (Ctenocephalides felis) and the Brown Dog Tick (Rhipicephalus sanguineus) in the Dog: Revised: Lab Project Number: 9251: P/215LT. Unpublished study prepared by Professional Labs and Research Services, Inc. 51 p.	43121115	MERIAL LIMITED	OLD	
810.3300	Everett, R.; Cunningham, J. (1993) A Comparative Evaluation of Two Treatment Regimes Using RM 1601 Spray for Control of the Cat Flea Ctenocephalides felis on the Dog: Revised: Lab Project Number: RMD 692: P/222LT. Unpublished study prepared by Agresearch Consultants, Inc. 40 p.	43121116	MERIAL LIMITED	OLD	
810.3300	McCall, J.; McTier, T. (1993) Laboratory Evaluation of RM 1601Spray for Control Dermacentor variabilis and Rhipecephalus sanguineus on the Dog: Lab Project Number: RM/TKS/93/1L: PS/229LT. Unpublished study prepared by TRS Labs, Inc. 18 p.	43121117	MERIAL LIMITED	OLD	
810.3300	Everett, R.; Cunniogham, J. (1993) An Investigation Study to Evaluate the Effect of Bathing of Laboratory Dogs on the Efficacy of RM1601 Spray: Revised: Lab Project Number: RMD 592: P/220LT. Unpublished study prepared by Agresearch Consultants, Inc. 43 p.	43121118	MERIAL LIMITED	OLD	
810.3300	Cruthers, L. (1993) Efficacy of RM1601C at 3 ml/kg and 6 ml/kg Against Ixodes scapularis/dammini Nymphs, Dermacentor variabilis Nymphs, Amblyomma americanum Nymphs, Rhipicephalus sanguineus Nymphs, and Ctenocephalides felides Adults Using Treated Dog Hair as the Testing Substrate: Revised: Lab Project Number: 9320: P/225LT. Unpublished study prepared by Professional Lab and Research Services, Inc. 28 p.	43121122	MERIAL LIMITED	OLD	
810.3300	Keister, D. ; Walker, K. (1994) Frontline Spray Treatment (RM1601C): Study Summaries. Unpublished study prepared by Rhone Merieux, Inc. 17 p.	43444901	MERIAL LIMITED	OLD	

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Ingredients: Fipronil, Novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Walker, K. (1995) Study Summaries: Frontline Spot Treatment (RM1601E/62). Unpublished study prepared by Rhone Merieux, Inc. 17 p.	43577701	MERIAL LIMITED	OLD	
810.3300	McCall, J. : MeTier, T. (1995) Positive Referenced and Untreated Controlled, Confirmatory Laboratory Trial of RM1601E SPOT-ON Formulation Applied to Dogs as 3 Weight Class Defined Volumes for the Conrol of the Cat Flea Ctenocephalides felis, the Brown Dog Tick Rhipicephalus sanguineus, and the American Dog Tick Dermacentor variabilis: Lab Project Numbers: RM/FLS – TKS/94/2L: RMI VSR – 249LT: PT – 249LT. Unpublished study prepared by TRS Labs, Inc. 41 p.	43577712	MERIAL LIMITED	OLD	
810.3300	Duke, K. (1996) Frontline Top Spot (RM1601E/62): Study Summaries. Unpublished study prepared by Rhone Merieux, Inc. 21 p.	43951701	MERIAL LIMITED	OLD	
810.3300	Duke, K. (1996) Frontline Spray Treatment: Experimental Use Permit: (Efficacy Data): Lab Project Number: PS-264CT: PS-265CT. Unpublished study prepared by Rhone Merieux, Inc. 10 p.	44088901	MERIAL LIMITED	OLD	
810.3300	Ahmed, Z. (2002) Study Summaries: Frontline Plus For Dogs. Unpublished study prepared by Merial. 40 p.	45612701	MERIAL LIMITED	PAY	
810.3300	Pengo, G.; Pollmeier, M.; Barrick, R. (2000) An Efficacy Study of Frontline Spray, Frontline Top Spot, and ML-2,095,988 509T, for the Treatment and Control of Trichodectes canis in the Dog: Final Report: Lab Project Number: PR&D 0022101, PR&D 0022I. Unpublished study prepared by Centro Veterinario Oriolo. 24 p.	45620501	MERIAL LIMITED	PAY	
810.3300	Marchiondo, A. (2001) PR & D 0024101: Frontline Spray/Frontline Spot-On/ML-2, 095, 988 509T/Dogs /Solution/Topical: Final Report: Lab Project Number: PR&D 0024101: PR&D 0024I. Unpublished study prepared by Stillmeadow, Inc. 29 p.	45620504	MERIAL LIMITED	PAY	
810.3300	Gaxiola, S.; Alva, R.; Irwin, J. (2001) PR & D 0052301: Frontline Spray/Frontline Spot-On/ML-2, 095, 988 509T/Dogs/ Solution/Topical: Final Report: Lab Project Number: PR&D 0052301, PR&D 00523. Unpublished study prepared by University of Sinaloa. 40 p.	45620505	MERIAL LIMITED	PAY	
810.3300	Pengo, G.; Pollmeier, M. (2000) Frontline Spray & Top Spot/ Dogs/Solution/Topical Clinial/Dose Confirmation/ Ectoparasites, Mites, Sarcoptes Scabiei var canis: Final Report: Lab Project Number: PR&D 0012901: PR&D 00129. Uapublished study prepared by Centro Veterinario Oriolo. 23 p.	45620506	MERIAL LIMITED	PAY	

Signature:	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	10/18/2012

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Date: October 18, 2012	EPA Reg No./File Symbol 53883-NEW	Page 6 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadeaa, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	

Ingredients: Fipronil, Novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Pengo, G.; Pollmeier, M. (2002) Study to Confirm the Efficacy of Fipronil Against Lice in Dogs Under Field Conditions: Final Report: Lab Project Number: PR&D 0037401. Unpublished study prepared by Centro Veterinario Oriolo. 21 p.	45628201	MERIAL LIMITED	PAY	
810.3300	McCall, J.; Alva, R.; Irwin, J.; et al. (2002) A Study to Evaluate the Efficacy of Frontline Plus for Control of Mosquitoes, Aedes aegypti, on Dogs: Final Report: Lab Project Number: PR&D 0055201. Unpublished study prepared by TRS Labs, Inc. 24 p.	45866902	MERIAL LIMITED	PAY	
810.3300	Dose Titration Probe with Novaluron Squeeze-Oas on Dogs Measuring Flea Egg Sterilization	48843211	Control Solutions, Inc.	OWN	
810.3300	Dose Confirmation for a 30 day Claim for a Novaluron Squeeze-On on Dogs Measuring Flea Egg Sterilization	48843212	Control Solutions, Inc.	OWN	
810.3300	Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*) on Dogs.	48843213	Control Solutions, Inc.	OWN	

Signature: Anne M Turnbough	Name and Title Anne Turnbough, Director, Regulatory Affairs	Date 10/18/2012

Information needed for a Notice of Receipt NOR:

1. EPA Reg Nos. = **53883-GRE (end-use)**

2. Chemical Name(s) = **Novaluron**

3. Proposed new uses* =
   - **Pet Spot on for Dogs**

4. Docket Number = **EPA-HQ-OPP-2012-0627**

5. Name of registrant and company address.

   Control Solutions, Inc.
   5903 Genoa Red Bluff
   Pasadena, TX 77507

6. Agency contact (as they want it to appear within the FR); phone number and email =

   - **Autumn Metzger, 703-305-5314, metzger.autumn@epa.gov**

about issues associated with integrating environmental justice concerns into EPA's outreach activities, public policies, and decision about science, regulatory, enforcement, and compliance issues related to environmental justice. Inquiries may be directed to Victoria Robinson, NEJAC Designated Federal Officer, U.S. EPA, 1200 Pennsylvania Avenue NW., (Mail Code 2201A), Washington, DC 20460.

Dated: July 13, 2012.

Cynthia Giles,

Assistant Administrator, Office of Enforcement and Compliance Assurance.

[FR Doc. 2012–23588 Filed 9–25–12; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

[Petition IV–2011–1; FRL–9734–2]

Clean Air Act Operating Permit Program; Petition for Objection to State Operating Permit for Tennessee Valley Authority's Shawnee Fossil Plant; McCracken County, KY

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of final order on petition to object to a state operating permit.

SUMMARY: Pursuant to Clean Air Act (CAA) Section 505(b)(2), the EPA Administrator signed an Order, dated August 31, 2012, denying a petition to object to a CAA title V operating permit issued by the Kentucky Division for Air Quality (KDAQ) to Tennessee Valley Authority for its Shawnee Fossil Plant (SFP) facility located in West Paducah, Kentucky. This Order constitutes a final action on the petition dated February 28, 2011, and submitted by the Environmental Integrity Project and the Southern Alliance for Clean Energy (Petitioners). Pursuant to sections 307(b) and 505(b)(2) of the CAA, a petition for judicial review of those parts of the Order that deny the petition may be filed in the United States Court of Appeals for the appropriate circuit within 60 days from the date this notice is published in the Federal Register.

ADDRESSES: Copies of the Order, the petition, and information relating thereto are on file at the following location: EPA Region 4; Air, Pesticides and Toxics Management Division; 61 Forsyth Street SW., Atlanta, Georgia 30303–8960. The Order is also available electronically at the following address: *http://www.epa.gov/region07/air/title5/petitiondb/petitions/shawnee_response2011.pdf.*

FOR FURTHER INFORMATION CONTACT: James Purvis, Air Permits Section, EPA Region 4, at (404) 562–9139 or *purvis.james@epa.gov.*

SUPPLEMENTARY INFORMATION: The CAA affords the EPA a 45-day period to review and, as appropriate, the authority to object to operating permits proposed by state permitting authorities under title V of the CAA, 42 U.S.C. 7661–7661f. Section 505(b)(2) of the CAA and 40 CFR 70.8(d) authorize any person to petition the EPA Administrator to object to a title V operating permit within 60 days after the expiration of the EPA's 45-day review period if the EPA has not objected on its own initiative. Petitions must be based only on objections to the permit that were raised with reasonable specificity during the public comment period provided by the state, unless the petitioner demonstrates that it was impracticable to raise these issues during the comment period or the grounds for the issues arose after this period.

Petitioners submitted a petition regarding SFP (received by the EPA on March 1, 2011), requesting that the EPA object to the CAA title V operating permit (#V–09–002 R1). Petitioners alleged that the permit was not consistent with the CAA for four primary reasons described in the petition. On August 31, 2012, the Administrator issued an Order denying the petition. In summary, the Petition was denied because the EPA interprets its regulations to limit the scope of petitions to object on permit revisions resulting from reopening for cause. The scope of petitions to object is limited to issues related to the parts of the permit for which the permitting authority has determined that cause to reopen exists. Because the Petitioners' objections apply to parts of the Shawnee Permit that are beyond the scope of the reopening for cause resulting in Permit Revision 1, the EPA is denying the Petition. The Order further explains the EPA's rationale for denying the petition.

Dated: September 17, 2012.

A. Stanley Meiburg,

Deputy Regional Administrator, Region 4.

[FR Doc. 2012–23690 Filed 9–25–12; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPP–2012–0390; FRL–9364–1]

Notice of Receipt of Pesticide Products; Registration Applications To Register New Uses

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces receipt of applications to register new uses for pesticide products containing currently registered active ingredients pursuant to the provisions of section 3(c) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended. This notice provides the public with an opportunity to comment on the applications.

DATES: Comments must be received on or before October 26, 2012.

ADDRESSES: Submit your comments, identified by docket identification (ID) number and the EPA Registration Number or EPA File Symbol of interest as shown in the body of this document, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.htm.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: A contact person is listed at the end of each registration application summary and may be contacted by telephone, email, or mail. Mail correspondence to the Antimicrobials Division (AD) (7510P) or Registration Division (RD) (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001. As part of the mailing address, include the contact person's name, division, and mail code.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. What should I consider as I prepare my comments for EPA?

1. *Submitting CBI.* Do not submit this information to EPA through regulations.gov or email. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD–ROM that you mail to EPA, mark the outside of the disk or CD–ROM as CBI and then identify electronically within the disk or CD–ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments.* When submitting comments, remember to:

i. Identify the document by docket ID number and other identifying information (subject heading, Federal Register date and page number).

ii. Follow directions. The Agency may ask you to respond to specific questions or organize comments by referencing a Code of Federal Regulations (CFR) part or section number.

iii. Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.

iv. Describe any assumptions and provide any technical information and/or data that you used.

v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.

vi. Provide specific examples to illustrate your concerns and suggest alternatives.

vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.

viii. Make sure to submit your comments by the comment period deadline identified.

II. Registration Applications

EPA has received applications to register new uses for pesticide products containing currently registered active ingredients. Pursuant to the provisions of FIFRA section 3(c)(4), EPA is hereby providing notice of receipt and opportunity to comment on these applications. Notice of receipt of these applications does not imply a decision by the Agency on these applications. For actions being evaluated under the Agency's public participation process for registration actions, there will be an additional opportunity for a 30-day public comment period on the proposed decision. Please see the Agency's public participation Web site for additional information on this process *http://www.epa.gov/pesticides/regulating/registration-public-involvement.html.* EPA received the following applications to register new uses for pesticide products containing currently registered active ingredients:

1. *EPA Registration Number:* 100–542. *Docket ID Number:* EPA–HQ–OPP–2012–0590. *Applicant:* Syngenta Crop Protection, LLC., P.O. Box 18300, Greensboro, NC 27419–8300. *Active ingredient:* Prometryn. *Product Type:* Herbicide. *Proposed Uses:* Dill and snap beans. Contact: Mindy Ondish, RD, (703) 605–0723, email address: *ondish.mindy@epa.gov.*

2. *EPA Registration Number:* 100–993. *Docket ID Number:* EPA–HQ–OPP–2012–0589. *Applicant:* Syngenta Crop Protection, LLC., P.O. Box 18300, Greensboro, NC 27419–8300. *Active ingredient:* Fomesafen. *Product Type:* Herbicide. *Proposed Use:* Vegetable soybean (edamame). Contact: Michael Walsh, RD, (703) 308–2972, email address: *walsh.michael@epa.gov.*

3. *EPA Registration Numbers:* 100–1017 and 100–1103. *Docket ID Number:* EPA–HQ–OPP–2012–0589. *Applicant:* Syngenta Crop Protection, LLC, P.O. Box 18300, Greensboro, NC 27419–8300. *Active ingredient:* Fomesafen. *Product Type:* Herbicide. *Proposed Use:* For formulation into an herbicide for use on cantaloupe, cucumber, pea (succulent), pumpkin, squash (Summer and Winter), watermelon, and vegetable soybean (edamame). Contact: Michael Walsh, RD, (703) 308–2972, email address: *walsh.michael@epa.gov.*

4. *EPA Registration Number:* 100–1374. *Docket ID Number:* EPA–HQ–OPP–2012–0704. *Applicant:* Syngenta Crop Protection, LLC., P.O. Box 18300, Greensboro, NC 27419–8300. *Active ingredient:* Sedaxane. *Product Type:* Fungicide. *Proposed Uses:* Seed treatment use on corn, popcorn, sorghum, pea and bean (dried shelled), and rapeseed. Contact: Heather Garvie, RD, (703) 308–0034, email address: *garvie.heather@epa.gov.*

5. *EPA Registration Number:* 100–1381. *Docket ID Number:* EPA–HQ–OPP–2012–0704. *Applicant:* Syngenta Crop Protection, LLC., P.O. Box 18300, Greensboro, NC 27419–8300. *Active ingredient:* Sedaxane. *Product Type:* Fungicide. *Proposed Use:* For formulation into a fungicide for use as a seed treatment for use on corn, popcorn, sorghum, pea and bean (dried shelled), and rapeseed. Contact: Heather Garvie, RD, (703) 308–0034, email address: *garvie.heather@epa.gov.*

6. *EPA Registration Number:* 264–666. *Docket ID Number:* EPA–HQ–OPP–2012–0588. *Applicant:* Bayer CropScience, LP., 2 T.W. Alexander Drive, P.O. Box 12014, Research Triangle Park, NC 27709. *Active ingredient:* Fenoxaprop-p-ethyl. *Product Type:* Herbicide. *Proposed Uses:* Post-emergence annual and perennial grass control in perennial ryegrass, tall fescue, and certain cultivars of annual ryegrass grown seed in Oregon, Utah, and Washington. Contact: Grant Rowland, RD, (703) 347–0254, email address: *rowland.grant@epa.gov.*

7. *EPA Registration Numbers:* 352–728, 352–729, 352–730, and 352–844. *Docket ID Number:* EPA–HQ–OPP–2012–0635. *Applicant:* DuPont Crop Protection, Stine-Haskell Research Center, P.O. Box 30, Newark, DE 19714. *Active ingredient:* Chlorantraniliprole. *Product Type:* Insecticide. *Proposed Uses:* Cereal grain group 15, except rice; forage, fodder; straw of cereal grain group 16; pome fruit group 11–10; and citrus fruit group 10–10. Contact: Jennifer Urbanski, RD, (703) 347–0156, email address: *urbonski.jennifer@epa.gov.*

8. *EPA File Symbol:* 6836–GLE. *Docket ID Number:* EPA–HQ–OPP–2012–0625. *Applicant:* Lonza, Inc., 90 Boroline Road, Allendale, NJ 07401. *Active ingredient:* 1-Bromo-3-chloro-5,5-dimethylhydantoin at 97.7%. *Product Type:* Disinfectant. *Proposed Use:* Drinking Water. Contact: Jaclyn Carl, AD, (703) 347–0213, email address: *carl.joclyn@epa.gov.*

9. *EPA Registration Number:* 7969–257. *Docket ID Number:* EPA–HQ–OPP–2012–0508. *Applicant:* BASF Corporation, 26 Davis Drive, Research Triangle Park, NC 27709. *Active ingredient:* Triticonazole. *Product Type:* Fungicide. *Proposed Uses:* Outdoor and

greenhouse ornamentals. Contact: Shaunta Hill, RD, (703) 347–8961, email address: *hill.shaunta@epa.gov.*

10. *EPA Registration Number:* 10163–209. *Docket ID Number: Docket ID Number:* EPA–HQ–OPP–2012–0357. *Applicant:* Gowan Company, 370 South Main Street, Yuma, AZ 85364. *Active ingredient:* Hexythiazox. *Product Type:* Insecticide. *Proposed Use:* For formulation into an insecticide for use on pepper and eggplant. Contact: Olga Odiott, RD, (703) 308–9369, email address: *odiott.olga@epa.gov.*

11. *EPA Registration Numbers:* 10163–250, 10163–251, and 10163–277. *Docket ID Number:* EPA–HQ–OPP–2012–0357. *Applicant:* Gowan Company, 370 South Main Street, Yuma, AZ 85364. *Active ingredient:* Hexythiazox. *Product Type:* Insecticide. *Proposed Uses:* Pepper and eggplant. Contact: Olga Odiott, RD, (703) 308–9369, email address: *odiott.olga@epa.gov.*

12. *EPA Registration Number:* 10163–277. *Docket ID Number:* EPA–HQ–OPP–2012–0623. *Applicant:* Gowan Company, 370 South Main Street, Yuma, AZ 85364. *Active ingredient:* Hexythiazox. *Product Type:* Insecticide. *Proposed Use:* Sorghum. Contact: Olga Odiott, RD, (703) 308–9369, email address: *odiott.olga@epa.gov.*

13. *EPA File Symbol:* 53883–GRE. *Docket ID Number:* EPA–HQ–OPP–2012–0627. *Applicant:* Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507. *Active ingredient:* Novaluron. *Product Type:* Insecticide. *Proposed Use:* Pet Spot treatment for Dogs. Contact: Autumn Metzger, RD, (703) 305–5314, email address: *metzger.autumn@epa.gov.*

14. *EPA File Symbol:* 59639–RTO. *Docket ID Number:* EPA–HQ–OPP–2011–0357. *Applicant:* Valent U.S.A. Corporation, P.O. Box 8025, Walnut Creek, CA 94596. *Active ingredient:* Fenpyrazamine. *Product Type:* Fungicide. *Proposed Uses:* Bushberry (subgroup 13–07B), caneberry (subgroup 13–07A), ginseng, and pistachio. Contact: Gene Benbow, RD, (703) 347–0235, email address: *benbow.gene@epa.gov.*

15. *EPA Registration Numbers:* 59639–150 and 59639–152. *Docket ID Number:* EPA–HQ–OPP–2010–0217. *Applicant:* Valent U.S.A. Corporation, P.O. Box 8025, Walnut Creek, CA 94596. *Active ingredient:* Clothianidin. *Product Type:* Insecticide. *Proposed Uses:* To amend an existing tolerance for crop subgroup 8–10B to 0.7 ppm. Contact: Marianne Lewis, RD, (703) 308–8043, email address: *lewis.marianne@epa.gov.*

16. *EPA Registration Number:* 59639–173. *Docket ID Number:* EPA–HQ–OPP–2010–0217. *Applicant:* Valent U.S.A. Corporation, P.O. Box 8025, Walnut Creek, CA 94596. *Active ingredient:* Clothianidin. *Product Type:* Insecticide. *Proposed Uses:* Expansion of crop groupings to receive the new fruiting vegetable crop group 8–10 and pome fruits crop group 11–10. Contact: Marianne Lewis, RD, (703) 308–8043, email address: *lewis.marianne@epa.gov.*

17. *EPA Registration Number:* 62719–416. *Docket ID Number:* EPA–HQ–OPP–2012–0520. *Applicant:* Dow AgroSciences LLC., 9330 Zionsville Road, Indianapolis, IN 46268. *Active ingredient:* Fenbuconazole. *Product Type:* Fungicide. *Proposed Use:* Pepper. Contact: Erin Malone, RD, (703) 347–0253, email address: *malone.erin@epa.gov.*

18. *EPA Registration Numbers:* 81880–2, 81880–15, and 81880–18. *Docket ID Number:* EPA–HQ–OPP–2012–0586. *Applicant:* Canyon Group LLC., c/o Gowan Company, 370 South Main St., Yuma, AZ 85364. *Active ingredient:* Halosulfuron-methyl. *Product Type:* Herbicide. *Proposed Uses:* Caneberry (subgroup 13–07A) and artichoke. Contact: Maggie Rudick, RD, (703) 347–0257, email address: *rudick.maggie@epa.gov.*

List of Subjects

Environmental protection, Pesticides and pests.

Dated: September 19, 2012.

Daniel J. Rosenblatt,

Acting Director, Registration Division, Office of Pesticide Programs.

[FR Doc. 2012–23736 Filed 9–25–12; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPP–2012–8736; FRL–9362–2]

Registration Review; Pesticide Dockets Opened for Review and Comment

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA is opening the public comment period for several registration reviews. Registration review is EPA's periodic review of pesticide registrations to ensure that each pesticide continues to satisfy the statutory standard for registration, that is, the pesticide can perform its intended function without unreasonable adverse effects on human health or the environment. Registration review dockets contain information that will assist the public in understanding the types of information and issues that the Agency may consider during the course of registration reviews. Through this program, EPA is ensuring that each pesticide's registration is based on current scientific and other knowledge, including its effects on human health and the environment. This document announces the Agency's intent not to open a registration review docket for bitertanol (case #6007), tridemorph (case #8009), and bethoxazin (case #5110). These pesticides do not currently have any actively registered pesticide products and are not, therefore, scheduled for review under the registration review program.

DATES: Comments must be received on or before November 26, 2012.

ADDRESSES: Submit your comments identified by the docket identification (ID) number for the specific pesticide of interest provided in the table in Unit III.A., by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.htm.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT:

For pesticide specific information contact: The Chemical Review Manager identified in the table in Unit III.A. for the pesticide of interest.

For general information contact: Kevin Costello, Pesticide Re-evaluation Division (7508P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001; telephone number: (703) 305–5026; fax number: (703) 308–8090; email address: *costello.kevin@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

This action is directed to the public in general, and may be of interest to a

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

June 19, 2012

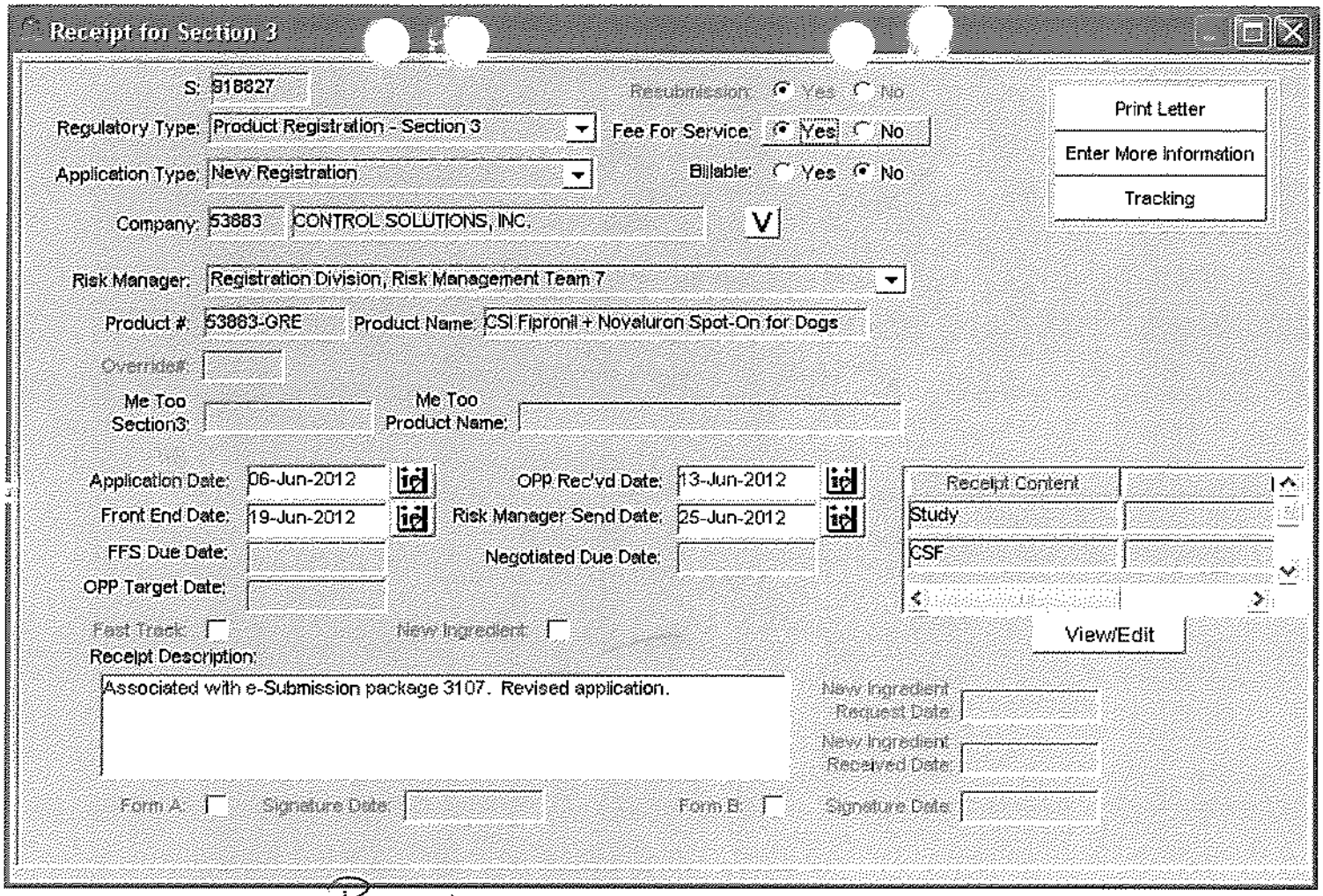
OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

CONTROL SOLUTIONS, INC.
5903 GENOA-RED BLUFF ROAD
PASADENA, TX 77507-1041

Report of Analysis for Compliance with PR Notice 11-03

Thank you for your submittal of 07-JUN-12. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 11-03. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.



Resubmission

~~Resub to fix GD~~ — ~~this is PRIA~~ —

needs to be Coded

& entered into OPPIN *

Autumn

not sure why this was separated from the jacket??

CSI
CONTROL
SOLUTIONS
Incorporated
A Makhteshim-Agan Company

June 18, 2012

Geri McCann and Adrienne Turner
Office of Pesticide Programs (7504P) (REGFEE)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: CD Containing the Application for Pesticide Registration for CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-GRE)

Dear Ms. McCann and Ms. Turner:

Please find enclosed a CD that contains a revised Application for Pesticide Registration for CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-GRE). Included on this CD is:

- Transmittal Document (revised to correct the MRID numbers for the Primary Eye and Primary Dermal Irritation studies);
- Application for Pesticide Registration (EPA Form 8570-1);
- Confidential Statement of Formula (EPA Form 8570-4);
- Formulator's Exemption Statement (EPA Form 8570-27);
- Certification with Respect to Citation of Data (EPA Form 8570-34);
- Data Matrix (EPA Form 8570-35) - EPA and Public Versions;
- Product Label;
- Child Resistant Packaging (CRP) Certification Statement for both CRP Suppliers;
- Letter of Authorization to cite CRP data on file with EPA;
- Submission of EPA Pesticide Registration Improvement Act Information;
- PRIA Category R260, Payment Confirmation Receipt; and
- Copies of the Supporting Studies.

Should you have any questions regarding this CD, or any of the files contained within, please do not hesitate to contact me at aturnbough@controlsolutionsinc.com or at 281-892-2532.

Sincerely,

Anne M. Turnbough

Anne Turnbough Ph.D.
Director, Regulatory Affairs

Enclosures

PRIA 2 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

3/23/09

21 Day Screen Start Date: 6-6-12

Experts In-Processing Signature: MF Harrington Date 6-13-12 Fee Paid: Yes ✓

Division management contacted on issues No_____Yes _____Date _____

EPA Reg. Number: 53883-GRE	EPA Receipt Date: 6-6-12

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1)(link to form) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4) (Link to form)			X		
	a) All inerts (link to http://www.epa.gov/opprd001/inerts/), including fragrances, approved for the proposed uses (see Footnote A) Inerts approved for non-food Use	**yes** X	**no**			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) (Link to form) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	**yes**	**no**			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) (Link to form) completed and signed (N/A if source is unregistered or applicant owns the technical)			X		
5	**Data Matrix** (EPA Form 8570-35) (Link to form) both internal and external copies (PR 98-5) (Link to PR 98-5) completed and signed (N/A if 100% repack)			X		
	a) Selective Method (Fee category experts use)	**yes** X	**no**			
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label** (link to **http://www.epa.gov/oppfead1/labeling/lrm/**) **(Electronic labels on CD are encouraged and guidance is available)**(link to http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm#labels)			X		

7	**Is the data package consistent with PR Notice 86-5** (link to PRN 86-5)	X		
8	**Notice of Filing (link to http://www.epa.gov/pesticides/regulating/tolerance_petitions.htm) included with petitions (link to http://www.epa.gov/pesticides/regulating/tolerances.htm)**			X
9	**If applicable for conventional applications, reduced risk rationale (link to http://www.epa.gov/opprd001/workplan/reducedrisk.html)**			X
10	**Required Data (link to http://www.epa.gov/pesticides/regulating/data_requirements.htm) and/or data waivers. See Footnote C.**			
	a) List study (or studies) not included with application			

Comments:

Inerts Approved for Non-Food Use

Jacket Pass
N-03 Pass

PG

MRID 4884432

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses. If an unapproved inert is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses **even if a product is currently registered** by consulting the inert Web

site [link to http://www.epa.gov/opprd001/inerts/lists.html] and if the inert is not approved, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch [Link to http://www.epa.gov/oppbppd1/biopesticides/contacts_bppd.htm].

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information [link to http://www.epa.gov/opprd001/inerts/tips.pdf] must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R311, R312 or R313), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

Your e-submission to EPA (Reg. No. 53883-GRE)
Fiker Getachew to: aturnbough 06/18/2012 11:44 AM

Dear Dr. Turnbough,

This email is regarding your e-submission of 488432 for the registration of CSI Fipronil + Novaluron Spot-On for Dogs.. The following deficiency was found in this submission:

1. Study 48843207 and 08 the titles are switched on transmittal.

Please send a CD with the revised copy of the transmittal to the attention of Geri Mccann (mccann.geri@epa.gov) and Adrienne Turner (turner.adrienne@epa.gov). Also, please acknowledge the receipt of this email.

If you have any questions or require additional information, please do not hesitate to contact me.

Thank you.
Fiker Getachew
EPA Contractor
703-305-6472

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

June 12, 2012

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OPP Decision Number: D-465891
EPA File Symbol or Registration Number: 53883-GRE
Product Name: CSI Fipronil + Novaluron Spot-On for Dogs
EPA Receipt Date: 07-Jun-2012
EPA Company Number: 53883
Company Name: CONTROL SOLUTIONS, INC.

ANNE TURNBOUGH, PH.D.
CONTROL SOLUTIONS, INC.
5903 GENOA-RED BLUFF ROAD
PASADENA, TX 77507-1041

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: R260

NEW USE;NON-FOOD;INDOOR;

No additional payment is due at this time.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-9362.

Sincerely,

Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service

{918260Ë~

This package includes the following

- ◉ New Registration
- ○ Amendment

☑ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 7

Receipt No. S- 918260

EPA File Symbol/Reg. No. 53883-GRE

Pin-Punch Date: 6/6/2012

☐ This item is NOT subject to FFS action.

Action Code:

Requested: R260

Granted: R260

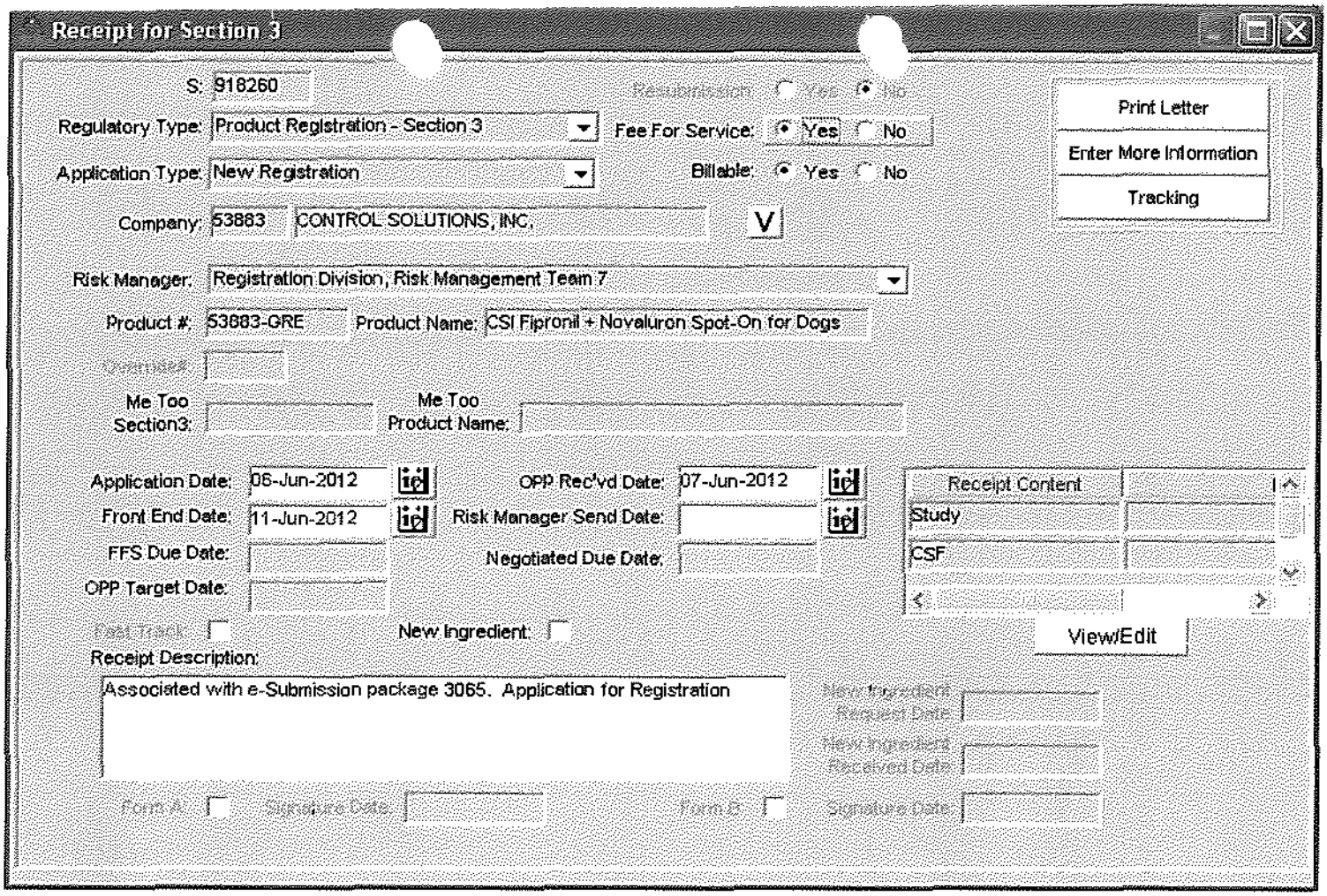
Amount Due: $ 11,577

Parent/Child Decisions:

☒ Inert Cleared for Intended Use ☒ Uncleared Inert in Product

Reviewer:_____ Date:_____

Remarks:



Pages 162-163 Claimed confidential by submitter

CSI
CONTROL
SOLUTIONS
incorporated
A Mukhteshim-Agan Company

June 06, 2012

John Hebert, PM7
Office of Pesticide Programs (7504P) (REGFEE)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: CD Containing the Application for Pesticide Registration for CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-~~NEW~~ GRE)

Dear Mr. Hebert:

Please find enclosed a CD that contains the Application for Pesticide Registration for CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-NEW). Included on this CD is:

- Transmittal Document;
- Application for Pesticide Registration (EPA Form 8570-1);
- Confidential Statement of Formula (EPA Form 8570-4);
- Formulator's Exemption Statement (EPA Form 8570-27);
- Certification with Respect to Citation of Data (EPA Form 8570-34);
- Data Matrix (EPA Form 8570-35) - EPA and Public Versions;
- Product Label;
- Child Resistant Packaging (CRP) Certification Statement for both CRP Suppliers;
- Letter of Authorization to cite CRP data on file with EPA;
- Submission of EPA Pesticide Registration Improvement Act Information;
- PRIA Category R260, Payment Confirmation Receipt; and
- Copies of the Supporting Studies.

Should you have any questions regarding this CD, or any of the files contained within, please do not hesitate to contact me at aturnbough@controlsolutionsinc.com or at 281-892-2532.

Sincerely,

Anne M Turnbough

Anne Turnbough Ph.D.
Director, Regulatory Affairs

Enclosures

5903 Genoa Red Bluff • Pasadena, TX 77507-1041 • www.controlsolutionsinc.com
281-892-2500 • Fax 281-892-2501 • 800-242-5562

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:

Control Solutions, Inc. (EPA Company No.53883)
5903 Genoa Red Bluff
Pasadena, TX 77507-1041

CONTACT PERSON (Return to)

Anne Turnbough
Control Solutions, Inc.
5903 Genoa Red Bluff
Pasadena, TX 77507-1041

REGULATORY ACTION SUPPORTED BY THIS PACKAGE:

This submission is to support the EPA registration application for the new end-use product CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-NEW).

SUBMITTAL DATE:

June 06, 2012

Volume	Study Title	MRID No.
1	Administrative Materials	48843200
2	Group A Product Chemistry for the End-Use Product CSI Fipronil + Novaluron Spot-On for Dogs	48843201
3	HPLC Method of Analysis for: Fipronil + Novaluron	48843202
4	NF Spot-On Product Chemistry (Group Product Properties)	48843203
5	NF Spot-On Acute Oral Toxicity (UDP) in Rats	48843204
6	NF Spot-On Acute Dermal Toxicity in Rats	48843205
7	Waiver Request of Requirement for Further Testing for Acute Inhalation Toxicity for Following CSI Products: CSI Fipronil + Novaluron Spot-On for Dogs; and CSI Fipronil + Novaluron Spot-On for Cats	48843206
8	Acute Eye Irritation Study in Rabbits	48843207
9	NF Spot-On Acute Dermal Irritation in Rabbits	48843208
10	NF Spot-On Skin Sensitization in Guinea Pigs	48843209
11	General Safety Evaluation of fipronil-Novaluron Spot-On in 8-Week-Old Puppies and Adult Dogs	48843210
12	Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization	48843211
13	Dose Confirmation for a 30 day Claim for a Novaluron Squeeze-On on Dogs Measuring Flea Egg Sterilization	48843212

Volume	Study Title	MRID No.
14	Comparative Efficacies of a Fipronil + Novaluron Spot-On and Frontline Plus against Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*) on Dogs.	48843213
15	Waiver Request for Group B Product Properties	48843214

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States Environmental Protection Agency Washington, DC 20460

☒ Registration ☐ Amendment ☐ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
53883-NEW	John Hebert	☒ None ☐ Restricted
4. Company/Product (Name) Control Solutions, Inc./CSI Fipronil + Novaluron Spot-on for Dogs	5.PM# 7	

5. Name and Address of Applicant *(Include ZIP Code)*
Control Solutions, Inc.
5903 Genoa Red Bluff
Pasadena, TX 77507

☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. No. _____

Product Name _____

Section II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of a registration application for the new end-use product CSI Fipronil + Novaluron Spot-on for Dogs.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging		Water Soluble Packaging	2. Type of Container
☒ Yes* ☐ No	☒ Yes ☐ No		☐ Yes ☒ No	☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag
***Certification must be submitted**	If "Yes" Unit Packaging wgt.	No. per Container	If "Yes" Package wgt.	No. per Container
	0.023 fl oz (0.67 ml) 0.045 fl oz (1.34 ml) 0.091 fl oz (2.68 ml) 0.136 fl oz (4.02 ml)	1, 2, 3, 4, 5, 6, 12, 24 vials		

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	0.023 fl oz (0.67 ml), 0.045 fl oz (1.34 ml), 0.091 fl oz (2.68 ml), 0.136 fl oz (4.02 ml)	☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☒ Other _____ ☐ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Anne Turnbough	Director, Regulatory Affairs	281-892-2532

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature	3. Title
BY: Anne M Turnbough	Director, Regulatory Affairs
4. Typed Name: Anne Turnbough	5. Date: 06/06/2012

Form approved. OMB No. 2070-0060, 2070- 2070-0107, 2070-0122, 2070-0164.

EPA

United States
Environmental Protection Agency
Washington, DC 20460

Formulator's Exemption Statement

(40 CFR 152.85)

Applicant's Name and Address	EPA File Symbol/Registration Number
Control Solutions, Inc. 5903 Genoa Red Bluff Pasadena, TX 77507-1041	53883-NEW
	Product Name CSI Fipronil + Novaluron Spot-On for Dogs
	Date of Confidential Statement of Formula *(EPA Form 8570-4)* 06/06/2012

As an authorized representative of the applicant for registration of the product identified above, I certify that:

(1) This product contains the following active ingredient(s):

Fipronil
Novaluron

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging another product which contains that active ingredient which is registered under FIFRA Section 3, is purchased by us from another person and meets the requirements of 40 CFR section 158.50(e)(2) or (3).

(3) Indicate by checking (A) or (B) below which paragraph applies:

☑ (A) An accurate Confidential Statement of Formula *(EPA FORM 8570-4)* for the above identified product is attached to this statement. That formula statement indicates, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1).

OR

☐ (B) The Confidential Statement of Formula (CSF)(EPA Form 8570-4) referenced above and on file with the EPA is complete, current, an accurate and contains the information required on the current CSF.

(4) The following active ingredients in this product qualify for the formulator's exemption.

Source

Active Ingredient	Product Name	Registration Number
Fipronil [redacted]	[redacted]	[redacted]
Fipronil [redacted]	[redacted]	[redacted]
Fipronil [redacted]	[redacted]	[redacted]
Fipronil [redacted]	[redacted]	[redacted]
Novaluron [redacted]	[redacted]	[redacted]

Signature	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	06/06/2012

EPA Form 8570-27 (Rev. 06-2004)

Copy 1 – EPA
Copy 2 - Applicant copy

Product ingredient source information may be entitled to confidential treatment

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Control Solutions, Inc., 5903 Genoa Red Bluff Pasadena, TX 77507	EPA Registration Number/File Symbol 53883-NEW
Active Ingredient(s) and/or representative test compound(s) Fipronil and Novaluron	Date June 06, 2012
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor non-food	Product Name CSI Fipronil + Novaluron Spot-On for Dogs

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).	☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Anne M Turnbough	June 06, 2012	Anne Turnbough, Director, Regulatory Affairs

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version.

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: June 06, 2012	EPA Reg No./File Symbol 53883-NEW	Page 1 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	

Ingredients: Fipronil, Novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1700, 830.1750	Group A Product Chemistry	48843201	Control Solutions, Inc.	OWN	
830.1800	Enforcement analytical method	48843202	Control Solutions, Inc.	OWN	
830.6302, 830.6303, 830.6304, 830.6313, 830.6315, 830.7100, 830.7300	Group B Product Properties	48843203	Control Solutions, Inc.	OWN	
830.6314, 830.6316, 830.6317, 830.6319, 830.6320, 830.6321, 830.7520	Waiver Request for Group B Product Properties	48843214	Control Solutions, Inc.	OWN	
830.6317, 830.6320	Storage stability and corrosion characteristics	To be conducted	Control Solutions, Inc.	OWN	
870.1100	Acute oral toxicity	48843204	Control Solutions, Inc.	OWN	
870.1200	Acute dermal toxicity	48843205	Control Solutions, Inc.	OWN	
870.1300	Acute inhalation toxicity	48843206	Control Solutions, Inc.	OWN	
870.2400	Primary eye irritation	48843207	Control Solutions, Inc.	OWN	
870.2500	Primary dermal irritation	48843208	Control Solutions, Inc.	OWN	
870.2600	Dermal sensitization	48843209	Control Solutions, Inc.	OWN	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.67 mL Capacity	48703501	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 1.34 mL Capacity	48703502	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 2.68 mL Capacity	48652701	Horizon Valley Generics, Inc.	PER	
40 CFR 157	Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 4.02 mL Capacity	48703503	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	
NA	Child Resistant Packaging Study Test Summary Report: Thermoforme Blister Pack for Pipettes of 0.5 mL Capacity, 0.67 mL Capacity, 1.34 mL Capacity, 2.68 mL Capacity, 4.02 mL Capacity	48703504	Chanelle Pharmaceuticals Manufacturing Ltd.	PER	

Signature:	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	06/06/2012

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401 M Street, S.W.
WASHINGTON, D.C. 20460

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Date: June 06, 2012	EPA Reg No./File Symbol 53883-NEW	Page 2 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	
Ingredients: Fipronil, Novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
NA	Use of One Tube 1x Child Resistant Unit Packaging Data (Child and Senior) to Support All Unit Configurations for Fipronil Based Spot-On Registrations	48614201	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze On 0.67ml White Applicator with Orange Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48614202	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze On 1.34ml White Applicator with Green Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48614203	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 2.68ml White Applicator with Red Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Product, Inc.	48614204	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze On 4.02ml White Applicator with Blue Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48614205	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 0.67ml White Applicator with Orange Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48059803	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 1.34ml White Applicator with Green Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	4859804	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 2.68ml White Applicator with Red Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	4859805	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Dog Squeeze on 4.02ml White Applicator with Blue Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	4859806	Sergeant's Pet Care Products, Inc.	PER	
40 CFR 157	Evaluation of the Cat Squeeze On 0.5 ml White Applicator with Purple Label Indicator (3x), scissors to open – F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.	48650101	Sergeant's Pet Care Products, Inc.	PER	

Signature:	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	06/06/2012

Form Approved OMB No. 2070-0060

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401 M Street, S.W.
WASHINGTON, D.C. 20460

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Date: June 06, 2012	EPA Reg No./File Symbol 53883-NEW	Page 3 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	

Ingredients: Fipronil, Novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.7200	General Safety Evaluation of fipronil-Novaluron Spot-on in 8-Week-Old Puppies and Adult Dogs	48843210	Control Solutions, Inc.	OWN	
870.7200	Arnaud, J.; Consalvi, P. (1993) Assessment of Tolerance of a 0.25% RM 1601 Spray Formulation in Dogs at 3, 9, and 15 ml/kg When Applied 6 times to the Haircoat at 28 Day Intervals: Revised: Lab Project Number CLI138. Unpublished study prepared by Rhone Merieux, Inc. 69 p.	43121110 ?	MERIAL LIMITED	OLD	
870.7200	Arnaud, J.; Consalvi, P. (1993) Domestic Animal Safety: Assessment of the Tolerance of a 0.25% RM 1601 Spray in Nursing Puppies Administered Twice at a 28 Day Interval at a Dose Rate of 6 ml/kg: Revised: Lab Project Number CLI 180. Unpublished study prepared by Rhone Merieux, Inc. 32 p.	43121111 ?	MERIAL LIMITED	OLD	
870.7200	Schwartz, E. (1994) Domestic Animal Safety Study of RM1601C Topical Spray (Frontline Spray Treatment) in Juvenile Dogs: Lab Project Number: 94423: PS-232DAS. Unpublished study prepared by White Eagle Toxicology Labs. 171 p.	43444905	MERIAL LIMITED	OLD	
870.7200	Walker, K. (1995) Discussion in Support of Bridging Domestic Animal Safety Data on Frontline Spray Treatment to Frontline Spot Treatment Data Package. Unpublished study prepared by Rhone Merieux, Inc. 6 p.	43577711 ✓	MERIAL LIMITED	OLD	
870.7200	Powell, L.; Paffett, R. (1995) Domestic Animal Safety Study by Topical Administration to Dogs: Fipronil Spot Treatment (RM 1601E): Lab Project Number: MRX 23/950406. Unpublished study prepared by Huntingdon Research Centre, Ltd. 219 p.	43863802	MERIAL LIMITED	OLD	
810.3300	Everett, R.; Cunningham, J. (1993) A Dose Titration Study to Determine the Optimal Spray Concentration of RM 1601 for Long Term Control of the Cat Flea Ctenocephalides felis and the Brown Dog Tick Rhipicephalus sanguineus in the Dog: Revised: Lab Project Number: RMD 292: P/214LT. Unpublished study prepared by Agresearch Consultants. 53 p.	43121114 ✓	MERIAL LIMITED	OLD	

Signature:	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	06/06/2012

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Ingredients: Fipronil, Novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Cruthers, L. (1993) Product Performance: A Dose Confirmation Study to Verify the Optimal Spray Concentration of RM 1601 for Long Residual Control of the Cat Flea (Ctenocephalides felis) and the Brown Dog Tick (Rhipicephalus sanguineus) in the Dog: Revised: Lab Project Number: 9251: P/215LT. Unpublished study prepared by Professional Labs and Research Services, Inc. 51 p.	43121115	MERIAL LIMITED	OLD	
810.3300	Everett, R.; Cunningham, J. (1993) A Comparative Evaluation of Two Treatment Regimes Using RM 1601 Spray for Control of the Cat Flea Ctenocephalides felis on the Dog: Revised: Lab Project Number: RMD 692: P/222LT. Unpublished study prepared by Agresearch Consultants, Inc. 40 p.	43121116	MERIAL LIMITED	OLD	
810.3300	McCall, J.; McTier, T. (1993) Laboratory Evaluation of RM 1601Spray for Control Dermacentor variabilis and Rhipecephalus sanguineus on the Dog: Lab Project Number: RM/TKS/93/IL: PS/229LT. Unpublished study prepared by TRS Labs, Inc. 18 p.	43121117	MERIAL LIMITED	OLD	
810.3300	Everett, R.; Cunningham, J. (1993) An Investigation Study to Evaluate the Effect of Bathing of Laboratory Dogs on the Efficacy of RM1601 Spray: Revised: Lab Project Number: RMD 592: P/220LT. Unpublished study prepared by Agresearch Consultants, Inc. 43 p.	43121118	MERIAL LIMITED	OLD	
810.3300	Cruthers, L. (1993) Efficacy of RM1601C at 3 ml/kg and 6 ml/kg Against Ixodes scapularis/dammini Nymphs, Dermacentor variabilis Nymphs, Amblyomma americanum Nymphs, Rhipicephalus sanguineus Nymphs, and Ctenocephalides felides Adults Using Treated Dog Hair as the Testing Substrate: Revised: Lab Project Number: 9320: P/225LT. Unpublished study prepared by Professional Lab and Research Services, Inc. 28 p.	43121122	MERIAL LIMITED	OLD	
810.3300	Keister, D. ; Walker, K. (1994) Frontline Spray Treatment (RM1601C): Study Summaries. Unpublished study prepared by Rhone Merieux, Inc. 17 p.	43444901	MERIAL LIMITED	OLD	

Signature	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	06/06/2012

Form Approved OMB No. 2070-0060

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Ingredients: Fipronil, Novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Walker, K. (1995) Study Summaries: Frontline Spot Treatment (RM1601E/62). Unpublished study prepared by Rhone Merieux, Inc. 17 p.	43577701	MERIAL LIMITED	OLD	
810.3300	McCall, J. : McTier, T. (1995) Positive Referenced and Untreated Controlled, Confirmatory Laboratory Trial of RM1601E SPOT-ON Formulation Applied to Dogs as 3 Weight Class Defined Volumes for the Conrol of the Cat Flea Ctenocephalides felis, the Brown Dog Tick Rhipicephalus sanguineus, and the American Dog Tick Dermacentor variabilis: Lab Project Numbers: RM/FLS – TKS/94/2L: RMI VSR – 249LT: PT – 249LT. Unpublished study prepared by TRS Labs, Inc. 41 p.	43577712	MERIAL LIMITED	OLD	
810.3300	Duke, K. (1996) Frontline Top Spot (RM1601E/62): Study Summaries. Unpublished study prepared by Rhone Merieux, Inc. 21 p.	43951711	MERIAL LIMITED	OLD	
810.3300	Duke, K. (1996) Frontline Spray Treatment: Experimental Use Permit: (Efficacy Data): Lab Project Number: PS-264CT: PS-265CT. Unpublished study prepared by Rhone Merieux, Inc. 10 p.	44088901	MERIAL LIMITED	OLD	
810.3300	Ahmed, Z. (2002) Study Summaries: Frontline Plus For Dogs. Unpublished study prepared by Merial. 40 p.	45612701	MERIAL LIMITED	PAY	
810.3300	Pengo, G.; Pollmeier, M.; Barrick, R. (2000) An Efficacy Study of Frontline Spray, Frontline Top Spot, and ML-2,095,988 509T, for the Treatment and Control of Trichodectes canis in the Dog: Final Report: Lab Project Number: PR&D 0022101, PR&D 00221. Unpublished study prepared by Centro Veterinario Oriolo. 24 p.	45620501	MERIAL LIMITED	PAY	
810.3300	Marchiondo, A. (2001) PR & D 0024101: Frontline Spray/Frontline Spot-On/ML-2, 095, 988 509T/Dogs /Solution/Topical: Final Report: Lab Project Number: PR&D 0024101; PR&D 00241. Unpublished study prepared by Stillmeadow, Inc. 29 p.	45620504	MERIAL LIMITED	PAY	
810.3300	Gaxiola, S.; Alva, R.; Irwin, J. (2001) PR & D 0052301: Frontline Spray/Frontline Spot-On/ML-2, 095, 988 509T/Dogs/ Solution/Topical: Final Report: Lab Project Number: PR&D 0052301, PR&D 00523. Unpublished study prepared by University of Sinaloa. 40 p.	45620505	MERIAL LIMITED	PAY	
810.3300	Pengo, G.; Pollmeier, M. (2000) Frontline Spray & Top Spot/ Dogs/Solution/Topical Clinial/Dose Confirmation/ Ectoparasites, Mites, Sarcoptes Scabiei var canis: Final Report: Lab Project Number: PR&D 0012901: PR&D 00129. Unpublished study prepared by Centro Veterinario Oriolo. 23 p.	45620506	MERIAL LIMITED	PAY	

Signature: Anne M Turnbough	Name and Title Anne Turnbough, Director, Regulatory Affairs	Date 06/06/2012

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: June 06, 2012	EPA Reg No./File Symbol 53883-NEW	Page 6 of 6
Applicant's/Registrant's Name & Address Control Solutions, Inc., 5903 Genoa Red Bluff, Pasadena, TX 77507	Product: CSI Fipronil + Novaluron Spot-on for Dogs	
Ingredients: Fipronil, Novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Pengo, G.; Pollmeier, M. (2002) Study to Confirm the Efficacy of Fipronil Against Lice in Dogs Under Field Conditions: Final Report: Lab Project Number: PR&D 0037401. Unpublished study prepared by Centro Veterinario Oriolo. 21 p.	45628201	MERIAL LIMITED	PAY	
810.3300	McCall, J.; Alva, R.; Irwin, J.; et al. (2002) A Study to Evaluate the Efficacy of Frontline Plus for Control of Mosquitoes, Aedes aegypti, on Dogs: Final Report: Lab Project Number: PR&D 0055201. Unpublished study prepared by TRS Labs, Inc. 24 p.	45866902 ✓	MERIAL LIMITED	PAY	
810.3300	Dose Titration Probe with Novaluron Squeeze-Ons on Dogs Measuring Flea Egg Sterilization	48843211	Control Solutions, Inc.	OWN	
810.3300	Dose Confirmation for a 30 day Claim for a Novaluron Squeeze-On on Dogs Measuring Flea Egg Sterilization	48843212	Control Solutions, Inc.	OWN	
810.3300	Comparative Efficacies of a Fipronil + Novaluron Spot-on and Frontline Plus against Fleas (*Ctenocephalides felis*) and Ticks (*Rhipicephalus sanguineus*) on Dogs.	48843213	Control Solutions, Inc.	OWN	

Signature:	Name and Title	Date
Anne M Turnbough	Anne Turnbough, Director, Regulatory Affairs	06/06/2012

CSI
CONTROL
SOLUTIONS
Incorporated
A Makhteshim-Agan Company

June 06, 2012

John Hebert, PM 7
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: Child Resistant Packaging Certification
CSI Fipronil + Novaluron Spot–On for Dogs
EPA File Symbol 53883-NEW

Dear Mr. Hebert:

I certify that the packaging used for the following product meets the standards of 40 CFR 157.32, including the revised standards in 16 CFR 1700.15(b), when tested by the revised testing procedures in 16 CFR 1700.20, as published in 60 FR 37710 (July 21, 1995):

- CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-NEW)

Control Solutions, Inc. (CSI, 5903 Genoa Red Bluff, Pasadena, TX 77507-1041, EPA Company Number 53883), is submitting this child resistant packaging certification statement to support the new end-use product registration application for CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-NEW). This certification statement is based on data submitted to EPA by Sergeant's Pet Care Products, Inc. and Klocke Verpackungs-Service GMBH for their respective child resistant packaging.

The data to support CRP packaging by Sergeant's Pet Care Products, Inc. are found under MRID 48614202, 48614203, 48614204, 48614205, 48059803, 48059804, 48059805 and 48059806. These data allow for CRP packaging configurations of 1X, 2X, 3X, 4X, 5X, 6X, 12X, and 24X in the fill weights 0.023 fl. oz. (0.67 ml), 0.045 fl. oz. (1.34 ml), 0.091 fl. oz. (2.68 ml), and 0.136 fl. oz. (4.02 ml). The CRP instructions for the Sergeant's Pet Care Product's, Inc. packaging is "How to Open: Remove product tube[s] [vial] from the package. [Separate one tube from the others.] Hold the tube [vial] with notched end pointing up and away from the face and body. Use scissors to cut off the narrow end at the notches along the line."

The data to support CRP packaging by Klocke Verpackungs-Service GMBH are found under MRID 48652701, 48703501, 48703502, and 48703503. These data allow for a CRP packaging configuration of 3X in the fill weights 0.023 fl. oz. (0.67 ml), 0.045 fl. oz. (1.34 ml), 0.091 fl. oz. (2.68 ml), and 0.136 fl. oz. (4.02 ml). The CRP instructions for the Klocke Verpackungs-Service GMBH packaging is "DIRECTIONS FOR OPENING PACKAGING: 1. Cut along scissor cut line to separate unit. 2. Turn unit over and cut corner at bulb end. 3. From cut corner, peel backing completely off from bottom to top. 4. Remove the applicator."

If you have any questions or need additional information, please contact me at aturnbough@controlsolutionsinc.com or at 281-892-2532.

Sincerely,

Anne M Turnbough

Anne Turnbough Ph.D.
Director, Regulatory Affairs

cc: Jim Messina, Exponent, Inc.
Matthew Feinberg, Exponent, Inc.
Terry McNamara, Exponent, Inc.

CSI
CONTROL
SOLUTIONS
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July 13, 2012

Rosalind Gross
Technical Review Branch
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Subject: Child Resistant Packaging
CSI Fipronil + Novaluron Spot–On for Dogs (EPA File Symbol 53883-GRE)

Dear Ms. Gross:

As per the request of the Agency, Control Solutions, Inc. (CSI, 5903 Genoa Red Bluff, Pasadena, TX 77507-1041, EPA Company Number 53883), certifies that the packaging used for the product CSI Fipronil + Novaluron Spot-On for Dogs (EPA File Symbol 53883-GRE) is the same, 100% identical packaging, as tested and approved by EPA, as Sergeant's Pet Care Products, Inc. and Klocke Verpackungs-Service GMBH for their respective child resistant packaging.

If you have any questions or need additional information, please contact me at aturnbough@controlsolutionsinc.com or at 281-892-2532.

Sincerely,

Anne M Turnbough

Anne Turnbough Ph.D.
Director, Regulatory Affairs

cc: John Herbert, EPA
Jim Messina, Exponent, Inc.
Matthew Feinberg, Exponent, Inc.
Terry McNamara, Exponent, Inc.

Sergeant's Pet Care Products, Inc.
10077 South 134th Street • Omaha, NE 68138-3710 • Telephone 402.938.7000 • Fax 402.938.7091 • www.sergeants.com

April 24, 2012

John Herbert (PM 7)
Document Processing Desk
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202

Subject: Letter of Authorization
Control Solutions, Inc. / Product Applications for Registration
CSI Fipronil + Novaluron Spot-On for Dogs, and
CSI Fipronil + Novaluron Spot-On for Cats

Dear Mr. Herbert:

This letter is to notify the U.S. Environmental Protection Agency that Sergeants Pet Care Products, Inc. (Sergeant's, EPA Company Number 2517) authorizes Control Solutions, Inc. (CSI, 5903 Genoa-Red Bluff Road, Pasadena TX 77507, EPA Company Number 53883) to cite child resistant packaging (CRP) data in support of its applications for registration of CSI Fipronil + Novaluron Spot-On for Dogs and CSI Fipronil + Novaluron Spot-On for Cats. These CRP data are proprietary to Sergeant's, and this letter does not confer ownership or exclusive rights of the data; other companies may rely on these data if authorized by Sergeant's. Below is a list of the CRP studies and MRID Numbers that CSI is authorized to cite.

Citation	MRID Number
Hoskins, K. (2011) Use of One Tube 1x Child Resistant Unit Packaging Data (Child and Senior) to Support All Unit Configurations for Fipronil Based Spot-On Registrations. Project Number: SERGEANT/S/02/09/11.	48614201
Ward, R. (2011) Evaluation of the Dog Squeeze On 0.67ml White Applicator with Orange Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc. Project Number: 1746/008.	48614202
Ward, R. (2011) Evaluation of the Dog Squeeze On 1.34ml White Applicator with Green Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc: Final Report. Project Number: 1746/009.	48614203
Ward, R. (2011) Evaluation of the Dog Squeeze on 2.68ml White Applicator with Red Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Product, Inc: Final Report. Project Number: 1746/010.	48614204
Ward, R. (2011) Evaluation of the Dog Squeeze On 4.02ml White Applicator with Blue Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc: Final Report. Project Number: 1746/011	48614205

Citation	MRID Number
Ward, R. (2010) Evaluation of the Cat Squeeze on 0.5ml White Applicator with Purple Label Indicator (3x), Scissors to open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc. Project Number: 1746/001.	48059503
Ward, R. (2010) Evaluation of the Dog Squeeze on 0.67ml White Applicator with Orange Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.: Final Report. Project Number: 1746/002	48059803
Ward, R. (2010) Evaluation of the Dog Squeeze on 1.34ml White Applicator with Green Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.: Final Report. Project Number: 1746/003	48059804
Ward, R. (2010) Evaluation of the Dog Squeeze on 2.68ml White Applicator with Red Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products. Inc.: Final Report. Project Number: 1746/004	48059805
Ward, R. (2010) Evaluation of the Dog Squeeze on 4.02ml White Applicator with Blue Label Indicator (3x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.: Final Report. Project Number: 1746/005.	48059806
Ward, R. (2010) Evaluation of the Cat Squeeze on 0.5mL White Applicator with Purple Label Indicator (3x), Scissors to Open - F= 1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.: Amended Final Report. Project Number: 1746/001.	48279601
Ward, R. (2011) Evaluation of the Cat Squeeze On 0.5ml White Applicator with Purple Label Indicator (1x), Scissors to Open - F=1 as a Poison Prevention Package for Sergeant's Pet Care Products, Inc.: Final Report. Project Number: 1746/007.	48613701
Evaluation of the Cat Squeeze On 0.5ml White Applicator with Purple Label indicator (3x), scissors to open -- F=1 as a poison prevention Package for Sergeants Pet Care Products, Inc. Perritt Study No. 1746-006	48650101

Please feel free to contact me with any questions via telephone at 402-938-7079 or via email at KHoskins@SERGEANTS.com.

Sincerely,

Kelly Hoskins
Director of Regulatory Affairs

cc: Anne Turnbough, Control Solutions, Inc.

KLOCKE VERPACKUNGS-SERVICE GMBH

April 24, 2012

John Herbert (PM 7)
Document Processing Desk
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202

Subject: Letter of Authorization
Control Solutions, Inc. / Product Applications for Registration
CSI Fipronil + Novaluron Spot-On for Dogs, and
CSI Fipronil + Novaluron Spot-On for Cats

Dear Mr. Herbert:

Please let this letter serve to notify the U.S. Environmental Protection Agency that Klocke Verpackungs-Service GMBH (Klocke) authorizes Control Solutions Inc. (CSI, 5903 Genoa-Red Bluff Road, Pasadena TX 77507, EPA Company Number 53883) to cite Child Resistant Packaging (CRP) data in support of applications for registrations of CSI Fipronil + Novaluron Spot-On for Dogs, and CSI Fipronil + Novaluron Spot-On for Cats products. These CRP data are proprietary to Klocke, and this letter does not confer ownership or exclusive rights of the data; other companies may rely on these data if authorized by Klocke. Below is a list of the CRP studies and MRID Numbers that CSI is authorized to cite.

Citation	MRID Number
Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.50 mL Capacity; Report No. KVS-201106	48771101
Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.67 mL Capacity; Report No. KVS-201107.	48703501
Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 1.34 mL Capacity; Report No. KVS-201108.	48703502
Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 2.68 mL Capacity; Report No. KVS-201104.	48652701
Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 4.02 mL Capacity; Report No. KVS-201109	48703503
Novosad, M. (2011) Child Resistant Packaging Study Test Summary Report: Thermoforme Blister Pack for Pipettes of 0.5 mL Capacity, 0.67 mL Capacity, 1.34 mL Capacity, 2.68 mL Capacity, 4.02 mL Capacity; Report No. KVS-201110	48703504

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Please direct any questions concerning this letter or the information contained herein to Richard Schwemmer at +33 3 88 45 33 13 or via email at richard.schwemmer@klocke.com.

Sincerely,

Dr. Magnus Zuther
C.E.O.

cc: Anne Turnbough, Control Solutions, Inc.

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Pages 183-208 Confidential Statement of Formula may be entitled to confidential treatment